

**SYNTHESIS AND PROPERTIES OF SOME NOVEL
CYCLOHEPTA [1,2;4,5] DITHIOPHENE SYSTEMS
AND RELATED COMPOUNDS**

Baruch Yom-Tov

Lund 1972

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SOME NOVEL CYCLOHEPTA[1,2;4,5]DITHIOPHENE SYSTEMS
AND RELATED COMPOUNDS

DISSERTATION

will be publicly discussed in the English language at the
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examen).

by

Baruch Yom-Tov, M.Sc., Gb

Lund 1972



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זכר וברכה

*To my mother
and father.
May their memory
be blessed.*



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CONTENTS

SUMMARY	10
---------	----

CHAPTER I, Introduction	14
-------------------------	----

Part 1. Literature survey	14
---------------------------	----

Part 2. Statement and discussion of the problem	17
---	----

- A. General synthetic postulations 17
- B. Stability of dithienotropylium ions 20
- C. Dithienotropylium ions in aromatic substitution 22
- D. Pharmacological derivatives 26

CHAPTER II	27
------------	----

- A. The synthesis of 4,5-dihydro-9H-cyclohepta-
[2,1-b;4,5-b']dithiophene-9-one (13) 27
- B. Synthesis of 8,9-dihydro-4H-cyclohepta-
[1,2-b;5,4-b']dithiophene-4-one (30) 34
- C. Synthesis of 8,9-dihydro-4H-cyclohepta-
[1,2-c;4,5-c']dithiophene-4-one (54) 39

CHAPTER III, The Wittig and Wadsworth-Horner syntheses
of some dithienylethylenes 48

- A. General synthetic conditions 48
- B. General physical properties of the
1,2-dithienylethylenes 49
- C. Mechanism and stereochemistry 50
- D. Interpretation of the results obtained
in phosphorane olefinations 56
- E. Stereochemistry in olefination -
Reactions of the diethyl thenylphosphonate ylids 63

CHAPTER IV, Dithienotropylium ions 68

- Part 1. Synthetic methods 68
- Part 2. Aromaticity of the dithienotropylium ions 71
 - A. Qualitative observations on the stability 71
 - B. Determination of the stability constants
for the dithienotropylium ions 76
- Part 3. Electrophilic substitution of
the dithienotropylium ions 80

CHAPTER V, On 3-methylaminopropylidene derivatives
of dihydro-cycloheptadithiophenes 86

A. 3-Dimethylaminopropylidene derivatives 86

B. 3-Monomethylaminopropylidene derivatives 89

CHAPTER VI, Experimental 92

Section A. Preliminary attempts towards
preparation of (13) 93

Section B. Starting materials for the
olefin syntheses 96

Section C. The Wittig and related syntheses 103

Section D. Carbonations and hydrogenations 111

Section E. Ketones 124

Section F. Cycloheptadithiophenes and
dithienotropylium ions 133

Section G. 3-N-Methylamino-propylidene derivatives
of the dihydrocycloheptadithiophenes 136

APPENDIX, The Mass Spectra of Some of the New Compounds 141

FORMULA INDEX of the new compounds 155

LITERATURE 165

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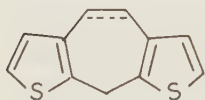
I am also grateful to Professor Bengt Aurivillius who so kindly informed me about the crystal structure of the dithienotropylium ions from his unpublished results of X-ray analyses, and to Astra Läkemedel AB for carrying out the pharmacological tests.

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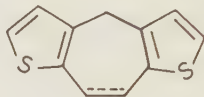
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SUMMARY

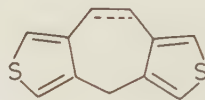
In Chapter I, after a brief literature survey and some statements about the synthetic approaches, some concepts motivating the syntheses of the cycloheptadithiophene systems (A), (B) and (C) are discussed.



(A)



(B)



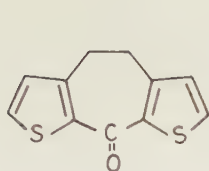
(C)

These concepts are, briefly, as follows:

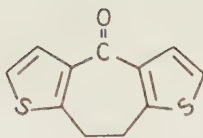
On the basis of purely geometrical arguments the tropylium ions derived from (A), (B) and (C), (A^+), (B^+) and (C^+), are assumed to be planar. With this basic assumption and application of simple resonance theory, a high stability for (A^+) and (B^+), in contrast to the low stability of benzenoid analogues, is suggested. Furthermore, the relative chemical reactivity of different positions in each of the ions (A^+), (B^+) and (C^+), in an aromatic substitution, was also predicted (Fig 7_I).

Chapter II deals mainly with the preparative side of this work.

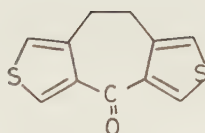
Novel syntheses of the ketones (13), (30) and (54) and some of their chloro derivatives (20), (33), (53) and (39) (see Formula Index) are broadly presented in this chapter.



(13)



(30)

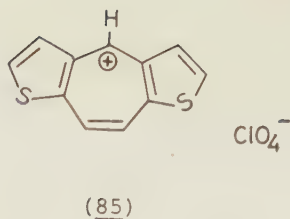
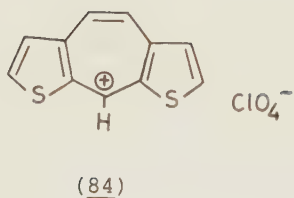


(54)

During the course of these syntheses, extensive use of the Wittig and Wadsworth-Horner olefinations was made in order to obtain the bromo-1,2-dithienyl ethylene intermediates. These bromides were carbonated through halogen-metal interconversion, and the ethylenic carboxylic acids which were obtained, were hydrogenated or vice versa. The saturated carboxylic acids were then cyclized to obtain the above mentioned dihydrocyclohepta-dithiophene-ones. In the course of the olefin syntheses, some remarkable features of these reactions were discovered, namely that certain modifications of the reactants altered drastically the isomer distribution of the products. Thus, in the use of the Wittig reaction to form the 1,2-dithienyl ethylenes, introduction of a halogen, ortho to the aldehyde function (of a thiophene aldehyde), always gave large amounts of the *cis* olefin. However, a bromo substituent on the thiophene moiety of the phosphorane had little effect on the stereochemistry. Similar behaviour was observed in the Wadsworth-Horner modification of these olefin syntheses. In this case substitution of a halogen on both the thiophene aldehyde, ortho position and/or the thiophene moiety of the phosphonate, caused an increase in *cis* production.

Explanation of these observations in the olefin syntheses is the subject of Chapter III.

In Chapter IV, the preparation of the dithieno tropylium perchlorates (84) and (85), starting from the corresponding ketones (13) and (30) is described. An attempt to prepare the isomeric tropylium ion derived from the system (C), (C⁺), starting from the ketone (54) was not fully successful. In an

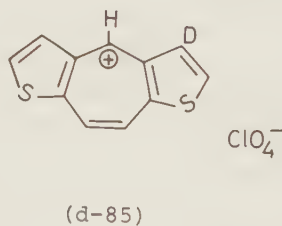
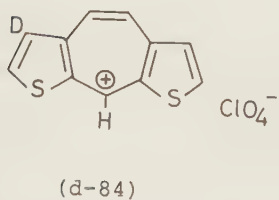


extensive investigation of chemical and physical properties of (84) and (85), the assumed coplanarity of these tropylium systems was established, both by spectroscopic properties and X-ray analysis.

The pK_R^+ values of these carbonium ions, as a measure of their stability, were also determined. The high positive values which were obtained, were in accord with the predicted high stability of these systems.

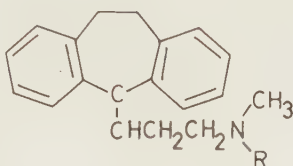
Finally, electrophilic substitution on (84) and (85) was performed. Both systems underwent deuteration in concentrated D_2SO_4 exclusively at their β -thiophenic positions. This was again according to the predictions by simple resonance theory as well as HMO calculations.

The positions of deuteration, which at first were assigned by nmr spectroscopy, were confirmed by an independent synthesis of the β -deuterated derivatives (d-84) and (d-85).



In the last chapter, the pharmacological aspects of these systems are dealt with.

Since compounds such as amitriptyline VII and nortriptyline (VIII) were found to be effective antidepressive drugs, it was interesting to see if the dithiophene analogues would have



(VII) $-R = -CH_3$

(VIII) $-R = -H$

similar properties. Ketones (13), (20), (30) and (39) were treated with 3-dimethylaminopropylmagnesium chloride in THF. Dehydration of the products furnished the thiophene analogues of (VII).

In an attempt to prepare the monomethyl derivatives (analogues of VIII) by demethylating the dimethylamino derivatives (see Scheme 2_V), only the nonchlorinated systems furnished the desired products (Scheme 3_V).

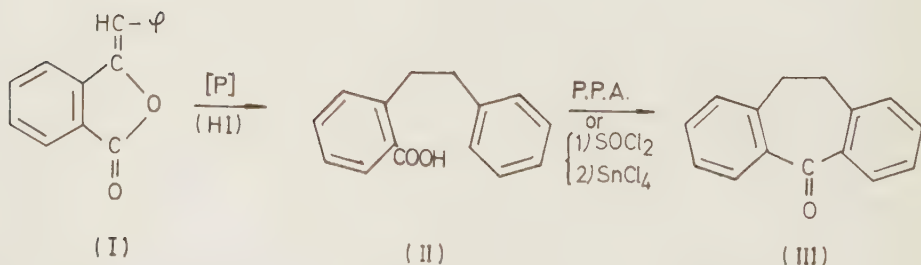
In preliminary pharmacological tests, these compounds showed biological activities similar to their dibenzo analogues.

Introduction

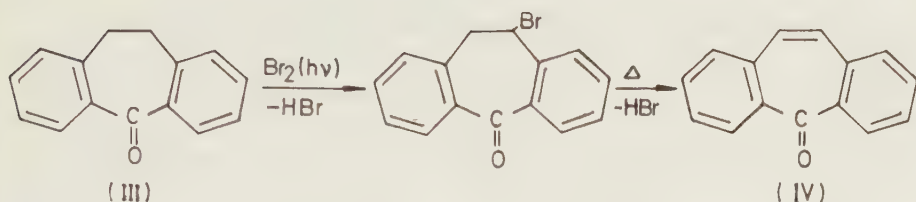
Part 1. Literature survey

Since the synthesis of 10,11-dihydro-5H-dibenzo[a,d]cyclohepta-5-one (III), which was reported (1950-51) by several authors (1-7), attention has been focussed on the properties of this tricyclic ring system and its derivatives. The tropylium ion derived from it has been studied and the pharmacological potentialities of large number of derivatives of this system have been explored.

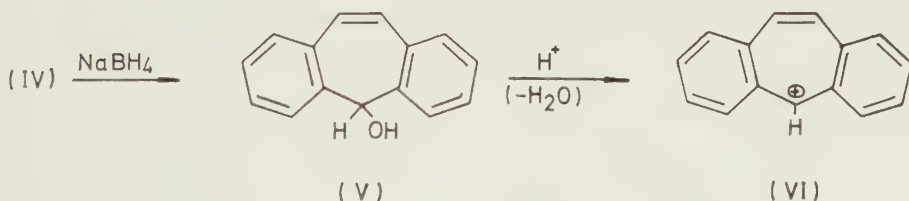
The dibenzocycloheptanone (III), which is the key starting material for these derivatives, has been best obtained by ring closure of the 2-phenethylbenzoic acid (II) (1,2,4,5,6), which in turn was prepared by reduction of benzylidene phthalide (I) by phosphorous in hydroiodic acid. Side chain bromination of (III), followed by spontaneous dehydrobromination, furnished



the unsaturated ketone 5H-dibenzo[a,d]cyclohepta-5-one (IV) (3,5).



Reduction of (IV) to the corresponding carbinol (V), followed by treatment in strong acid, furnished the dibenzo-[a,d]tropylium ion (VI).

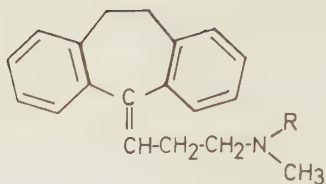


Berti (16), who was the first to obtain (VI) in this way, also determined its pK_R^+ as a measure of the stability of the carbonium ion, using the method of Deno et al. (17). This value was found to be $\text{pK}_\text{R}^+ = -3.7$, which was later corrected to $\text{pK}_\text{R}^+ = -1.9 \pm 0.1$ by Heilbronner et al. (25).

The discovery of tranquilizing properties of certain thiazine derivatives led to an extensive investigation of related tricyclic ring systems.

Among others, various 5-(N-alkylamino)-alkyl (10-14) and 5-(N-alkylamino)-alkylidene (8-14) derivatives have been synthesized and their biological properties have been investigated.

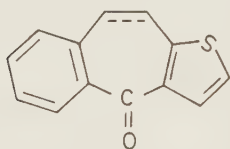
Some of these derivatives, such as amitriptyline (VII) (8,9) and nortriptyline (VIII) (15), have found their way to the market, as antidepressive drugs.



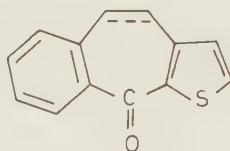
(VII) $-R = -CH_3$

(VIII) $-R = -H$

By replacing one benzene ring in ketone (III) or (IV) with a thiophene ring, three isomeric (dihydro)-benzocyclohepta-thiophene-ones are possible. Two of them, namely (9,10-dihydro)-4H-benzo[4,5]cyclohepta[1,2-b]thiophene-4-one (IX), and (4,5-dihydro)-10H-benzo[5,6]cyclohepta[2,1-b]thiophene-10-one (X), as well as a large number of alkyliden and alkyl amino

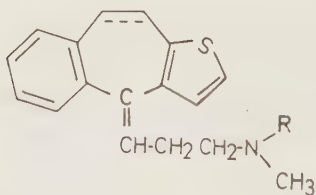


(IX)

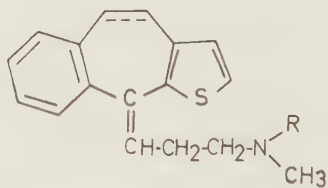


(X)

derivatives such as (XI) and (XII) have been reported by a group of Swiss workers (18,19).



(XI)



(XII)

$-R = -H, -CH_3$

Part 2. Statement and discussion of the problem

A. General synthetic postulations

In analogy with the dibenzocycloheptane system, which is represented by the dibenzo[a,d]cycloheptanone (III), we were interested in synthesizing some of the dithiophene analogues of the system.

Six isomeric dithiophene analogues of this ring system are possible.

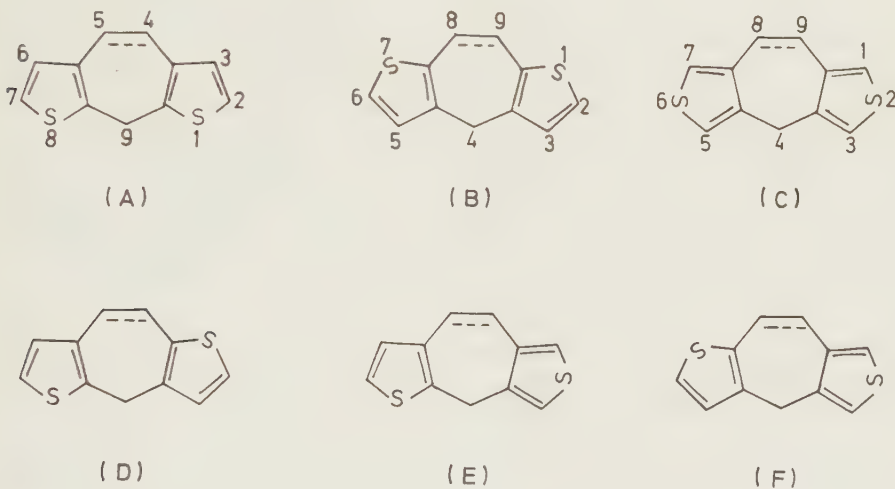


Figure 1_I

Preparations of three of the isomers, namely (A), (B) and (C) in Fig 1_I represented by the corresponding ketones:

(A): (4,5-dihydro)-9H-cyclohepta[2,1-b;4,5-b']dithiophene-9-one,
(B): (8,9-dihydro)-4H-cyclohepta[1,2-b;5,4-b']dithiophene-4-one,
(C): (8,9-dihydro)-4H-cyclohepta[1,2-c;4,5-c']dithiophene-4-one,
were undertaken. Some chloro derivatives of these ketones were also desirable. These systems could then be used to obtain both the thiophene analogues of the tropylium ion (VI) and some interesting pharmacological derivatives related to (VII) and (VIII).

A reasonable synthetic approach to these systems could involve the synthesis of monobromodithieno olefins (a), (b) and (c) in Fig 2_I, whose double bond could be saturated and

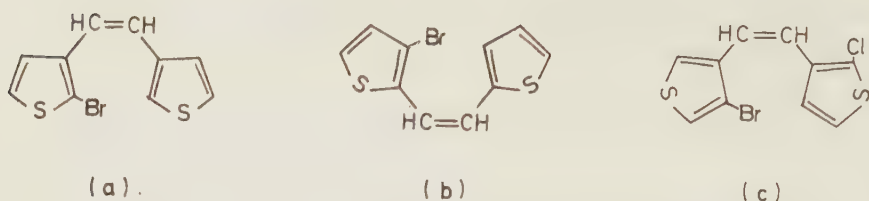


Figure 2_I

then converted to the carboxylic acid derivatives, through halogen-metal interconversion - followed by carbonation (or vice versa). Cyclization of the acids would then produce the desired systems (Fig 3_I).

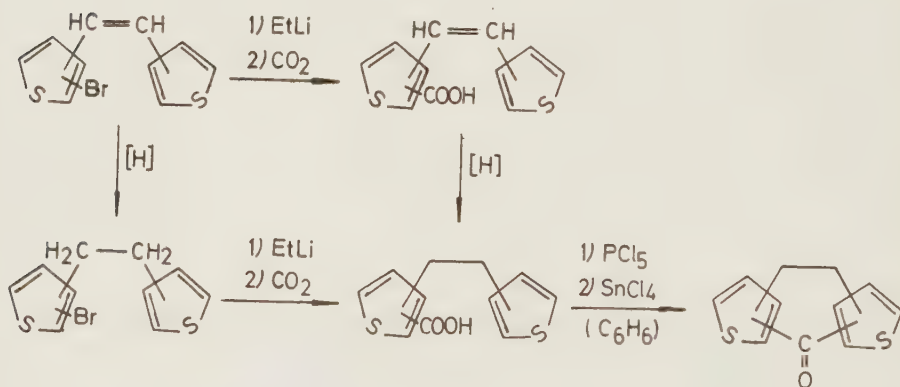


Figure 3_I

The dithienoethylene intermediates could be obtained easily by the Wittig olefin synthesis or the phosphonate olefin synthesis modification.

This synthetic approach would be advantageous not only because it would supply a convenient general route for the

synthesis of all the possible isomeric cycloheptadithiophene systems in Fig 1_I, but also there were good reasons to believe that, by adjustment of the reaction conditions, the Wittig olefinations would probably furnish substantial amounts of cis bromo-dithienoethylenes. Carbonation of these cis olefins followed by cyclization would reduce the synthesis of the cycloheptadithiophene-ones to a simple three-step reaction sequence as presented schematically in Fig 4_I, while otherwise

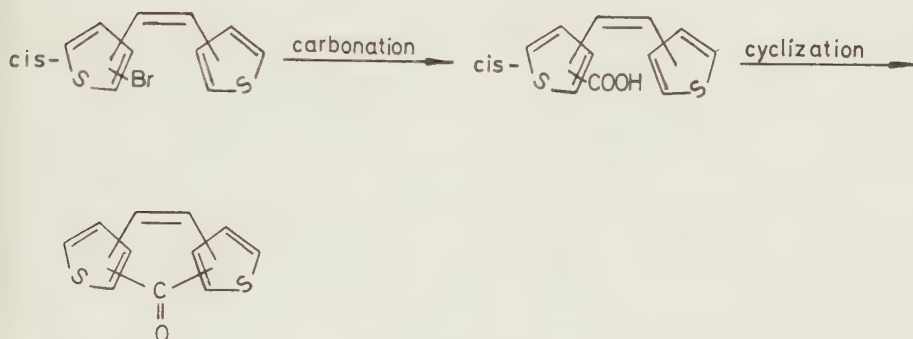


Figure 4_I

a multi-step reaction sequence involving side-chain bromination of the corresponding dihydrocycloheptadithiophene-one, followed by dehydrobromination, would be required (Fig 5_I).

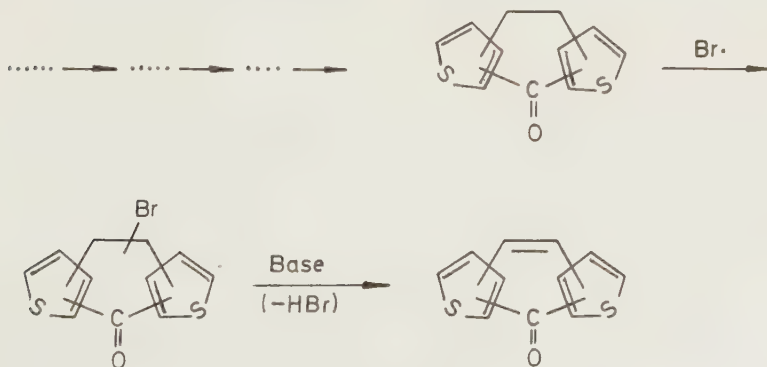


Figure 5_I

As will be seen in the discussion of synthetic methods (Chapter II), these predictions were more than justified. Thus not only almost all the synthetic objectives were achieved, but also, the numerous olefin syntheses which have been performed in this work supplied a better insight into the stereochemistry of olefin syntheses of this sort.

This aspect of the olefinations will be discussed separately in Chapter III.

B. Stability of dithienotropylium ions

The plethora of knowledge (20), which has been accumulated on the tropylium cation, since it was predicted in 1931 by Hückel (21) and obtained in 1954 by von Doering and Knox (22), reveals a rather curious fact. Namely, that condensing benzenoid rings to tropylium cation increases the acidity (decreases the pK_R^+) of the carbonium ion. This effect seems, at first sight, to be rather puzzling, since the apparent extension of the conjugated system would be expected to have a stabilizing effect on the carbonium ion, rather than the opposite.

Different explanations have been offered for this behavior. The stability decrease of tropylium cation, with annelation of a benzene ring, has been attributed by Berti (16) to "Many high-energy non-Kekulé structures, involved in the resonance of the ions of benzene homologues". However, it should be recalled here that the pK_R^+ in fact is the acidity constant of R^+ and the conjugated pseudobase ROH, namely the equilibrium constant for:



Therefore, in the examination of the effect of the substituent on the acidity of the tropylium ion, account must be taken of the effect of the substituent, both on the cation R^+ , and on the pseudobase ROH, conjugated with it.

From this point of view Heilbronner and coworkers (23) suggested that: "Benzene rings condensed with the tropylium ion, probably stabilize the uncharged cycloheptatriene system to a greater extent than the positively charged tropylium ring".

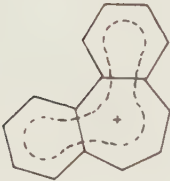
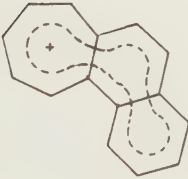
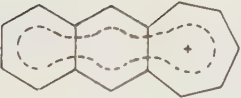
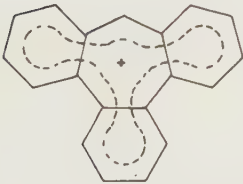
Cations	pK_R^+	Ref.
	+4.7	(22)
	+1.7 ± 0.1	(24)
	-2.9 ± 0.3	(25)
	-1.9 ± 0.1	(16)
	+2.2 ± 0.1	(23)
	+0.3 ± 0.1	(25)
	-7.4	(26)

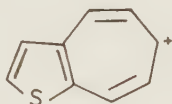
Figure 6_I

A concrete meaning for this general postulation concerning the benzene homologues of tropylium cation (Fig 6_I) can be realized in terms of distortion of the central cycloheptatrienylum ring from co-planarity.

The breakdown of co-planarity, probably arising from peri and/or ortho hydrogen interferences, and from angular strains (26), is directly related to the number of fused benzene rings as well as to the mode of fusion.

The reduced π - π interaction in the 7-carbon π -electron system of the benzene homologues prevents effective delocalization of the positive charge, and hence the cation exhibits a higher acidity than the planar nonsubstituted tropylium ion.

The tropylium ion condensed with a thiophene ring (XIII) was found to be much more stable ($pK_R^+ = 6.05$) (27) than the unsubstituted ($pK_R^+ = 4.7$) tropylium ion.



(XIII)

On the basis of purely geometrical arguments it may be concluded that b-annulation of thiophene ring has little effect on the co-planarity of the tropylium ion, since there must be little angular strain, and almost no neighbouring-hydrogen interferences occurring in this thienotropylium ion.

Therefore the higher stability of the thieno homologues of tropylium ion may be attributed to the more effective charge delocalization, which is associated with expansion of the planar conjugated system.

C. Dithienotropylium ions in aromatic substitution

Following this argument, with further extension of the conjugated system (XIII) by an additional thiophene ring (4,5-b' fused), an increase in stability would be expected.

Assuming planarity, two sets of resonance structures (A) and (B) for each of the b-annelated dithienotropyliums (Fig 7_I) may be written.

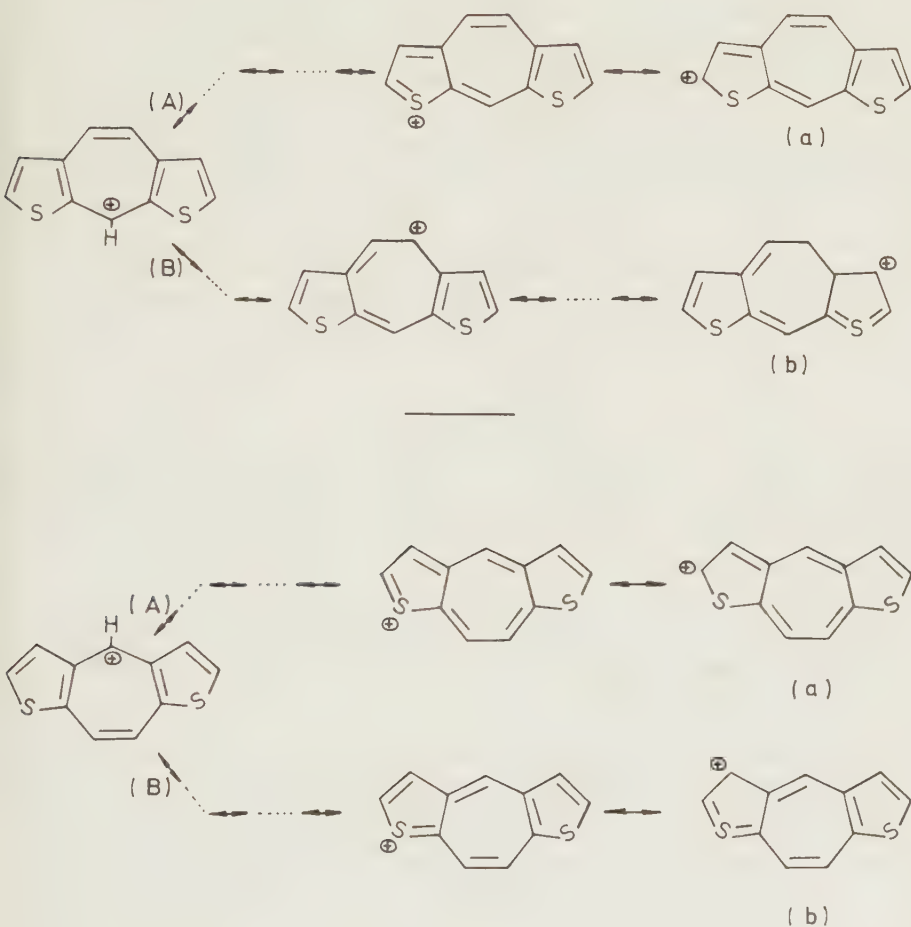
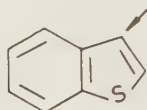


Figure 7_I

On the basis of varying contribution of resonance forms to the hybrid structure, a first approximation of chemical reactivity (towards electrophiles) for these systems can be made.

Generally speaking, the vacant positions on the central cycloheptenylium ring are more positive than the thiophenic ones.

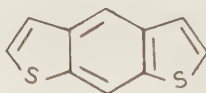
Therefore, the latter positions generally are more reactive. In comparing the resonances sets (A) and (B), since canonical forms (a) contain only single "short" C-S bond while the (b) resonance forms include also quadrivalent sulphur $\text{S}^{\equiv}$ (decet around the sulphur), the former forms contribute more to the respective hybrids than the latter (28). Therefore the thiophenic β -position in both systems should possess the highest electron density, which means they would be attacked most readily by electrophilic agents. This conclusion is consistent with the known fact that thionaphthene (XIV), which is isoelectronic with



(XIV)

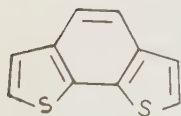
the b-annelated dithienocycloheptenylium systems, undergoes electrophilic attack exclusively on the β -thiophenic position (29).

The interesting feature about this conclusion is the parallel lines which can be drawn about aromaticity and aromatic substitutions for some other isoelectronic ring systems such as dithiaanthracene (XV) (30),

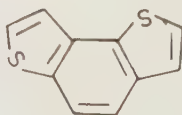


(XV)

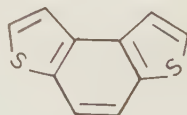
dithiaphenanthrenes (XVI), (XVII) and (XVIII) (31) as well as



(XVI)

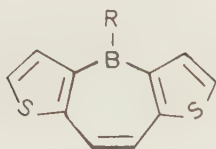


(XVII)

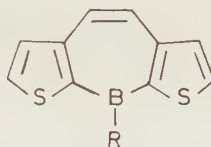


(XVIII)

dithienoborepines (XIX), which have been prepared (32) in these laboratories, and (XX) which is still under preparation (33).



(XIX)



(XX)

Somewhat more obscure will be the aromatic properties of c-annulated dithienocycloheptenylum system .

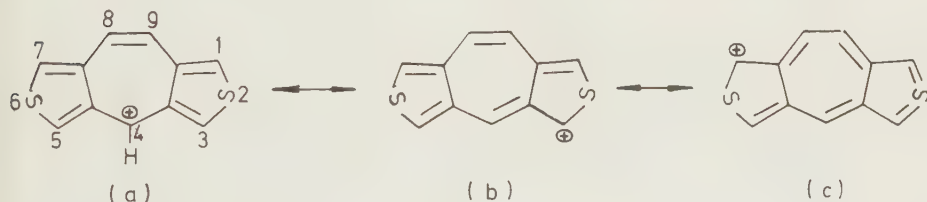


Figure 8_I

Due to the bond fixations associated with the classical form of thiophene, resonance form (a) (Fig 8_I) is the most important contributor to the hybrid system. Therefore, the central seven-membered ring is not a cycloheptatrienylum ion in the classical sense. This means, compared to the b-annulated systems, lower stability should be expected for such carbonium ions.

From the resonance forms (b) and (c), some prediction about the relative reactivities of the different positions of the system may be made. The canonical form (b) will be a more important contributor than (c), since (c) contains quadrivalent sulphur (28). Therefore, electrophilic attack should take place preferably on identical positions 1 and 7, which are the least positive positions in this system.

In view of the foregoing hypothetical conclusions concerning the chemical reactivity of dithienotropylium ions, which have been based on simple resonance considerations, it was interesting to see, how far these conclusions are consistent with the experimental results. Therefore, preparation and investigation of the three dithienotropylium ions, which were discussed in Figures 7_I and 8_I, were undertaken from the corresponding ketones (Fig 5_I).

D. Pharmacological derivatives

As already mentioned, compounds such as amitriptyline (VII) and nortriptyline (VIII) have shown good antidepressive properties. There was therefore good reason to believe that, in view of similar geometry and chemical properties, the dithiophene analogues would exhibit similar biological activities. Furthermore, it was hoped that the undesired biological side-effects which are often associated with the benzenoid tricyclic tranquilizing and antidepressive agents, would perhaps be eliminated or reduced, by substituting benzene with thiophene.

Preparation of some (3-methylamino-propyliden)-dihydro-cycloheptadithiophenes could then be accomplished practically by the same sequence of reactions which were used originally to obtain the dibenzo analogues (VII) and (VIII). This is shown schematically in Fig 9_I.

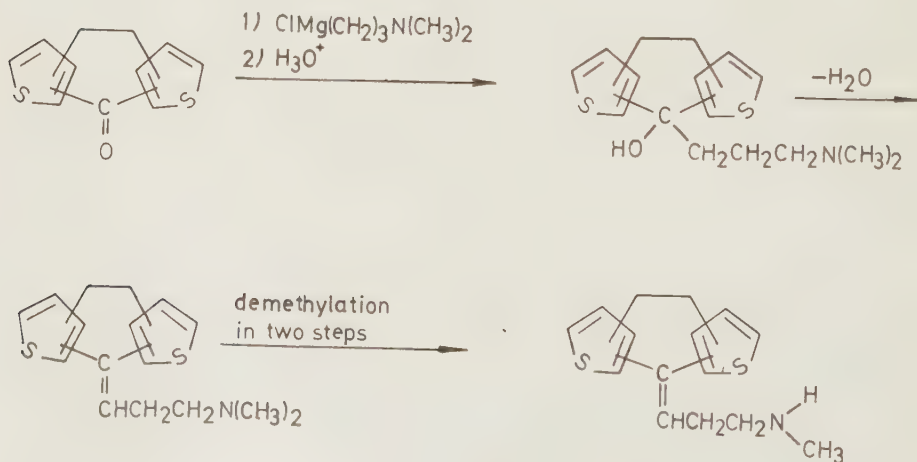


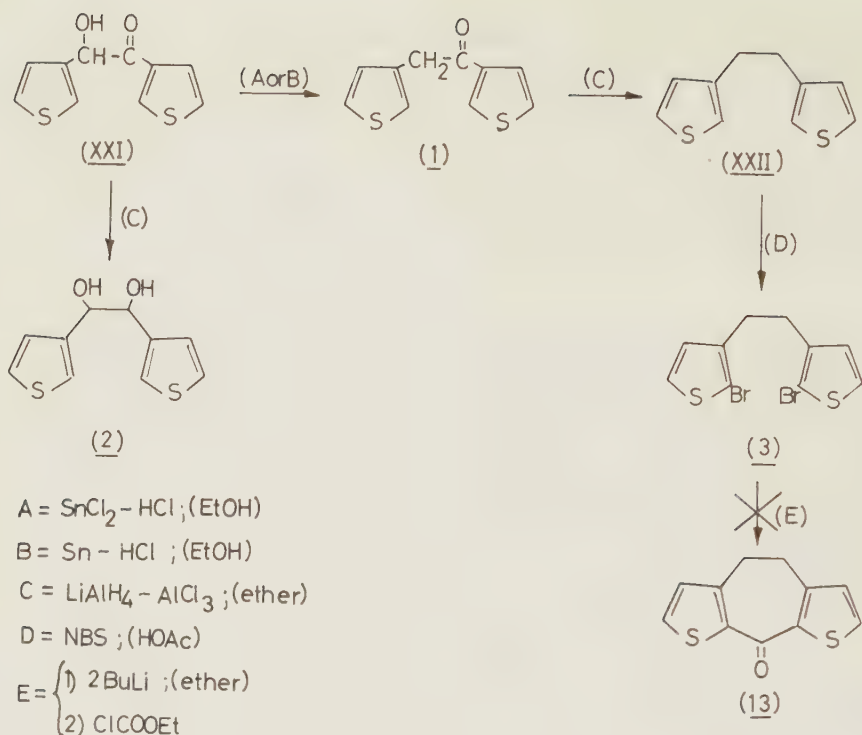
Figure 9_I

A. The synthesis of 4,5-dihydro-9H-cyclohepta[2,1-b;4,5-b']-dithiophene-9-one (13)

The first attempt to obtain this ketone was made when sym-di(3-thienyl)ethane (XXII) was brominated by N-bromosuccinimide (NBS) to give sym-di(2-bromo-3-thienyl)ethane (3) (35). The dilithium derivative of (3) was then allowed to react, at -70° , with ethylchloroformate. The oily, tar-like product which remained after the work-up did not show any substantial carbonyl-stretching absorption.

We concluded from this result that uncontrollable intermolecular reactions led to undefined products in this reaction.

Campaigne and LeSuer (34) obtained (XXII) in a Grignard coupling of 3-thienyl bromide. We prepared this substance by a different reaction route, which is summarized in Scheme 1_{II}. The compound 3,3'-thenoin (XXI) (34) was reduced to desoxythenoin (1) by tin powder or SnCl_2 in an EtOH solution of HCl (36,37). Further reduction of (1) by $\text{LiAlH}_4\text{-AlCl}_3$ in ether (38) eventually gave the product (XXII). Direct reduction of 3,3'-thenoin (XXI) by $\text{LiAlH}_4\text{-AlCl}_3$ led to sym-di(3-thienyl)ethane-diol (2) but not to (XXII), as expected (38).



Scheme 1_{II}

Since the reaction between the dilithium derivative of (3) and ethyl chloroformate failed to produce the desired ketone (13), this route was abandoned and the possibility of obtaining this ketone through ring closure of 1-(2-carboxy-3--thienyl)-2-(3'-thienyl)ethane (12) (Scheme 2_{II}) was considered. Attempts to obtain the bromo precursor, 1-(2-bromo-3-thienyl)-2-(3'-thienyl)ethane (9), by bromination of (XXII) with one equivalent of NBS led to a mixture of mono- and dibromo derivatives. In view of these difficulties, an unambiguous synthesis of the carboxylic acid intermediate, (12), seemed to be best achieved through either the Wittig (53) olefin synthesis or the Wadsworth-Horner (72,86) modification of this reaction.

As shown in Scheme 2_{II}, a mixture of cis and trans 1-(2-bromo-3-thienyl)-2-(3'-thienyl)ethylenes (7) and (8) was obtained by four different reaction routes, (C)₁, (C)₂, (D)₁ and (D)₂. All these reactions were carried out smoothly in dry DMF, at room temperature, with short reaction times (1-1.5 hr), and good yields. These yields varied from 70-75 % in cases where phosphonium salts were used, as in the routes (C)₁ and (D)₁, and 90 % when the phosphonates were used, as in the routes (C)₂, (D)₂.

As would be expected (39), the trans isomer was overwhelmingly predominant in the (C)₂ and (D)₂ routes, while a high percentage of cis isomer was obtained in (C)₁ and (D)₁ routes. Furthermore, a surprisingly higher percentage of cis isomer was observed in route (D)₁, where 2-bromo-3-thiophene aldehyde (48) was reacted with the 3-thenylidene phosphorane derived from 3-thenyltriphenylphenylphosphonium bromide (6), while in (C)₁, where the 3-thiophene aldehyde was not substituted, a lower ratio of cis isomer was obtained in the olefinic product. Even the phosphonate modifications (C)₂ and (D)₂ also showed this same tendency. In (D)₂, the cis ratio was slightly higher than that observed in (C)₂.

This trend appeared to be a general feature of all the syntheses of halo-substituted 1,2-dithienylethylenes which we carried out. That is, a higher cis ratio was always associated with the routes where a halo-substituted thiophene aldehyde was reacted with a thenylidene phosphorylid. This aspect of the olefin syntheses will be discussed in more detail in Chapter III.

The 2-bromo-3-thenyltriphenylphosphonium bromide (4) and its parent compound (6) were prepared in high yields by the reaction of triphenylphosphine with the corresponding thenyl bromides in benzene.

The diethyl(2-bromo-3-thenyl)phosphonate (5) and diethyl-3-thenyl phosphonate (XXV) (19) were obtained by heating 2-bromo-3-thenylbromide (XXIII) and 3-thenylbromide (XXIV) (34) with triethylphosphite, respectively.

The 1-(2-carboxy-3-thienyl)-2-(3'-thienyl)ethane (12) which is the key intermediate in the preparation of ketone (13), was obtained in two alternative ways: first, through the

hydrogenation of 1-(2-carboxy-3-thienyl)-2-(3'-thienyl)ethylenes (10) and/or (11), which in turn were obtained from the isomeric bromoethylenes (7) and/or (8) by halogen-metal exchange and carbonation, and secondly by the reverse sequence of steps, namely: carbonation of 1-(2-bromo-3-thienyl)-2-(3'-thienyl)ethane (9) which in turn was obtained from olefins (7) and/or (8) through homogeneous catalytic hydrogenation (40).

While (10) and/or (11) could either be reduced by sodium amalgam in EtOH or by homogeneous catalytic hydrogenation using tris-(triphenylphosphine)chlororhodium^I (T.T.Rh^ICl) (41) as the catalyst, bromides (7) and/or (8) could be saturated only through the catalytic method, since the carbon-bromine bond was easily cleaved by sodium-amalgam. Alternative 2 was found to be the more suitable for the preparation of acid (12), since the compound was obtained in a higher yield and in a purer form.

Finally, cyclization of carboxylic acid (12) gave the desired ketone 4,5-dihydro-9H-cyclohepta[2,1-b;4,5-b']dithiophene-9-one (13). We found the most convenient method of cyclization to be through the acid chloride intermediate, using SnCl₄. The advantages of this cyclization method in these systems over similar methods are mild reaction conditions, high yields, and short reaction times.

For pharmacological screening (see Chapter V) it was necessary to prepare some derivatives of 2-chloro-4,5-dihydro-9H-cyclohepta[2,1-b;4,5-b']dithiophene-9-one (20). The preparation of this ketone (Reaction Scheme 3_{II}) is very similar to that already described for the parent ketone (13).

It can be expected that a direct chlorination of (13) by chlorine or N-chlorosuccinimide (NCS) may give rise to a mixture of products.

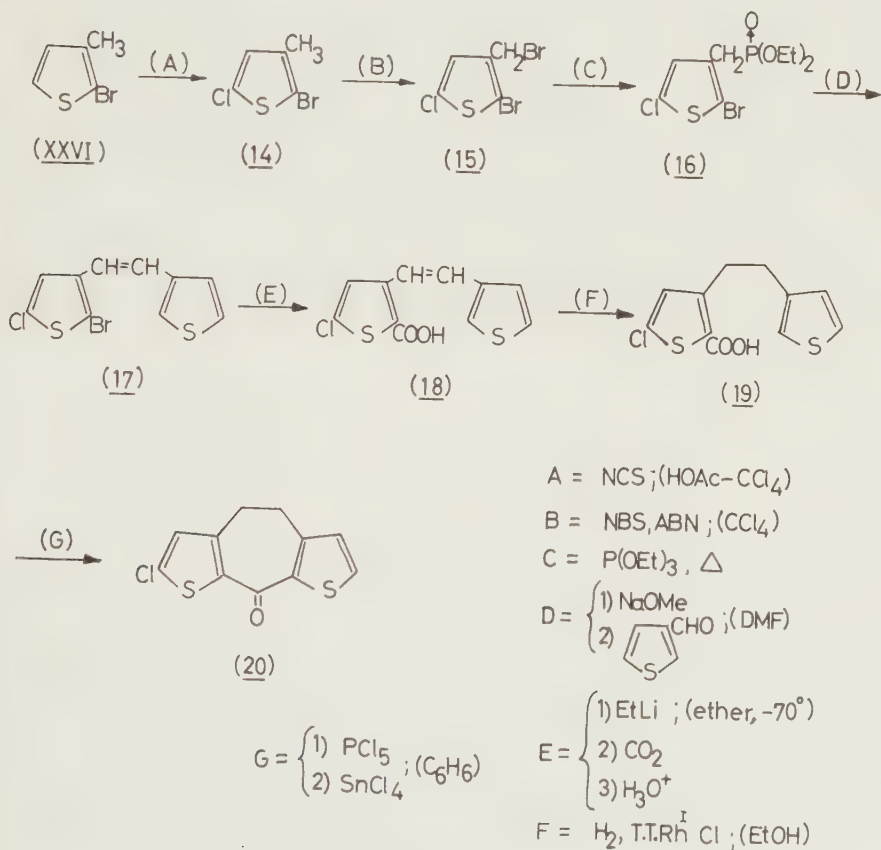
While the 2- and 7-positions in (13) are activated by the heteroatom, the carbonyl function deactivates these positions in preference to the 3- and 6-positions. On the other hand, the 3- and 6-positions are activated by the ethylenic bridge. The combination of these effects tends to equalize the chemical reactivity of the different thiophene positions toward electrophilic attack. Indeed, one attempt which was made to chlorinate (13) with one equivalent of NCS in acetic acid, resulted in an oily mixture of ketonic products, which could not be separated into its components. Therefore, further attempts to prepare (20) by direct chlorination of (13) were not made, and this compound was prepared according to the Reaction Scheme 3_{II} as described below. This route has the advantage of being an unequivocal synthesis.

The 2-bromo-3-methylthiophene (XXVI) was chlorinated by NCS in glacial acetic acid. Unlike the chlorination of bromothiophenes by Cl₂ in which chlorine may substitute nuclear bromine, in chlorination with NCS, this sort of attack was practically negligible and a good yield of 5-chloro-2-bromo-3-methylthiophene (14) was obtained. The other steps are shown in Scheme 3_{II}. Side-chain bromination (42) of (14) to obtain 5-chloro-2-bromo-3-bromomethylthiophene (15), the preparation of the corresponding phosphonate (16), and the syntheses of 1-(5-chloro-2-bromo-3-thienyl)-2-(3'-thienyl)ethylene (17) and the carboxylic acid 1-(5-chloro-2-carboxy-3-thienyl)-2-(3'-thienyl)ethylene (18), were all carried out by the same sequence of reactions which was used in the synthesis of analogous compounds in Scheme 2_{II}.

An attempt to saturate the olefinic double bond in (18) by sodium amalgam in EtOH failed to give the desired product,

apparently because of dechlorination. Therefore, the best hydrogenation method, in such a case, seemed to be hydrogenation with T.T.Cl Rh^I as catalyst.

Compound (18) was, therefore, hydrogenated by this method and the saturated carboxylic acid 1-(5-chloro-2-carboxy-3-thienyl)-2-(3'-thienyl)ethane (19) which was obtained could be cyclized to give the desired monochloro ketone (20) using nearly the same conditions that were used in cyclization of (12).



Scheme 3_{II}

B. Synthesis of 8,9-dihydro-4H-cyclohepta[1,2-b;5,4-b']-dithiophene-4-one (30)

The synthesis of this ketone was accomplished by a method similar to that used for (13). The sequence of reactions which was used in the synthesis of (30) are summarized in Scheme 4_{II}.

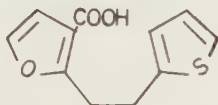
Reaction routes (C)₁ and (D)₁, in which phosphoranes derived from 3-bromo-2-thienyltriphenylphosphonium chloride (21) and 2-thienyltriphenylphosphonium chloride (23) were reacted with 2-thiophene aldehyde and 3-bromo-2-thiophene aldehyde respectively, gave cis 1-(3-bromo-2-thienyl)-2-(2'-thienyl)-ethylene (24) in substantial amounts. On the other hand, reaction of diethyl(3-bromo-2-thienyl)phosphonate (22), and diethyl(2-thienyl)phosphonate (XXIX) (18) with 2-thiophene aldehyde and 3-bromo-2-thiophene aldehyde, in routes (C)₂ and (D)₂ respectively, furnished mainly the trans olefin (25). Here again, as in the previous olefin syntheses, an increased amount of the cis isomer was observed in case where the reacting thiophene aldehyde had a bromo substituent ortho to its aldehyde function.

The compound 1-(3-carboxy-2-thienyl)-2-(2'-thienyl)ethane (29), which is the key substance for the synthesis of the ketone (30) and its derivative 2-chloro-8,9-dihydro-4H-cyclohepta[1,2-b;5,4-b']dithiophene-4-one (33), was obtained by two different routes. These were analogous to the reaction routes which have been discussed for the synthesis of the isomeric carboxylic acid (12) in Scheme 2_{II}. As shown in Scheme 4_{II} the lithium derivatives of (24) and/or (25), which were obtained through halogen-metal interconversion with EtLi in the usual manner, were carbonated to give the cis 1-(3-carboxy-2-thienyl)-2-(2'-thienyl)ethylene (27) and/or its trans isomer (28) respectively. A mixture of (27) and (28) could be also obtained, as shown in route E, directly from the reaction of the phosphonate (XXIX) with 3-carboxyl-2-thiophene aldehyde (43).

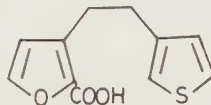
Finally, saturation of the olefinic double bonds in (27) and/or (28) either by homogeneous catalytic hydrogenation (40) or by reduction with sodium amalgam in EtOH gave the key intermediate (29). An alternative preparation which had some experimental advantages in terms of purer product and higher overall yield, consisted of homogeneous catalytic hydrogenation of (24) and/or (25). This gave 1-(3-bromo-2-thienyl)-2-(2'-thienyl)-ethane (26) in about 95 % yield, which was carbonated in the usual manner to give the compound (29).

In parallel to the cyclization of the carboxylic acids (12) and (19) (see Schemes 2_{II} and 3_{II}), a good yield of (30) was obtained through the action of SnCl₄ on the acyl chloride derivative of (29). The reaction conditions under which this cyclization was carried out, were practically the same as in the previous cyclizations of (12) and (19). In a cyclodehydration attempt of (29) by PPA, which was carried out at about 130° for 1.5 hrs, (30) was obtained in about 30 % yield.

From cyclizations of the saturated carboxylic acids (12), (19), (29), (XXX) (44) and (XXXI) (44), which have been



(XXX)



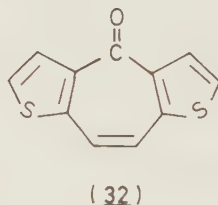
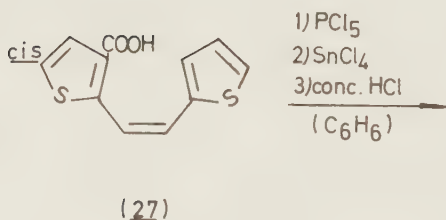
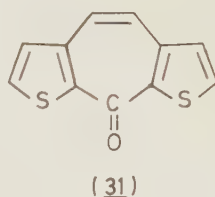
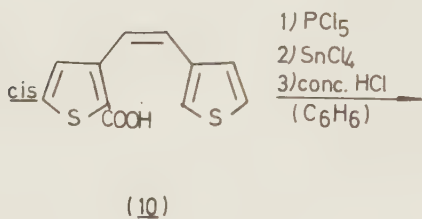
(XXXI)

carried out in this laboratory, we have observed the following: first, formation of the acyl chloride intermediate from the carboxylic acid and PCl₅, and its subsequent cyclization with SnCl₄ could in all cases be carried out in a one-pot reaction. Second, mild reaction conditions, short reaction times and high yields of cyclized product (>90 % in nearly all cases) were rather the rule than the exception.

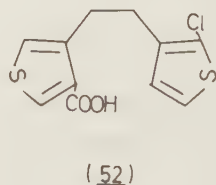
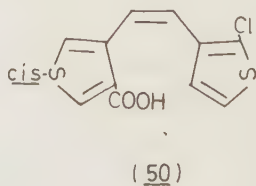
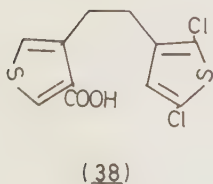
On the basis of these experimental observations, it is possible to state quite certainly that this is probably the most suitable cyclization method as well as other forms of Friedel-Crafts type reactions for thiophene positions, provided

that the position in question is not strongly deactivated by -I and -M effects of other substituents. The slight -M effect which the olefinic double bond in the cis carboxylic acids (10) and (27) exerts on the attacked sites did not prevent the cyclization of these two systems.

The ketones 9H-cyclohepta[2,1-b;4,5-b']dithiophene-9-one (31) and 4H-cyclohepta[1,2-b;5,4-b']dithiophene-4-one (32) were obtained in >80 % yield.



We have also attempted, by this method, the cyclization of the carboxylic acids (38), (50) and (52), whose syntheses are described in Part C of this chapter.

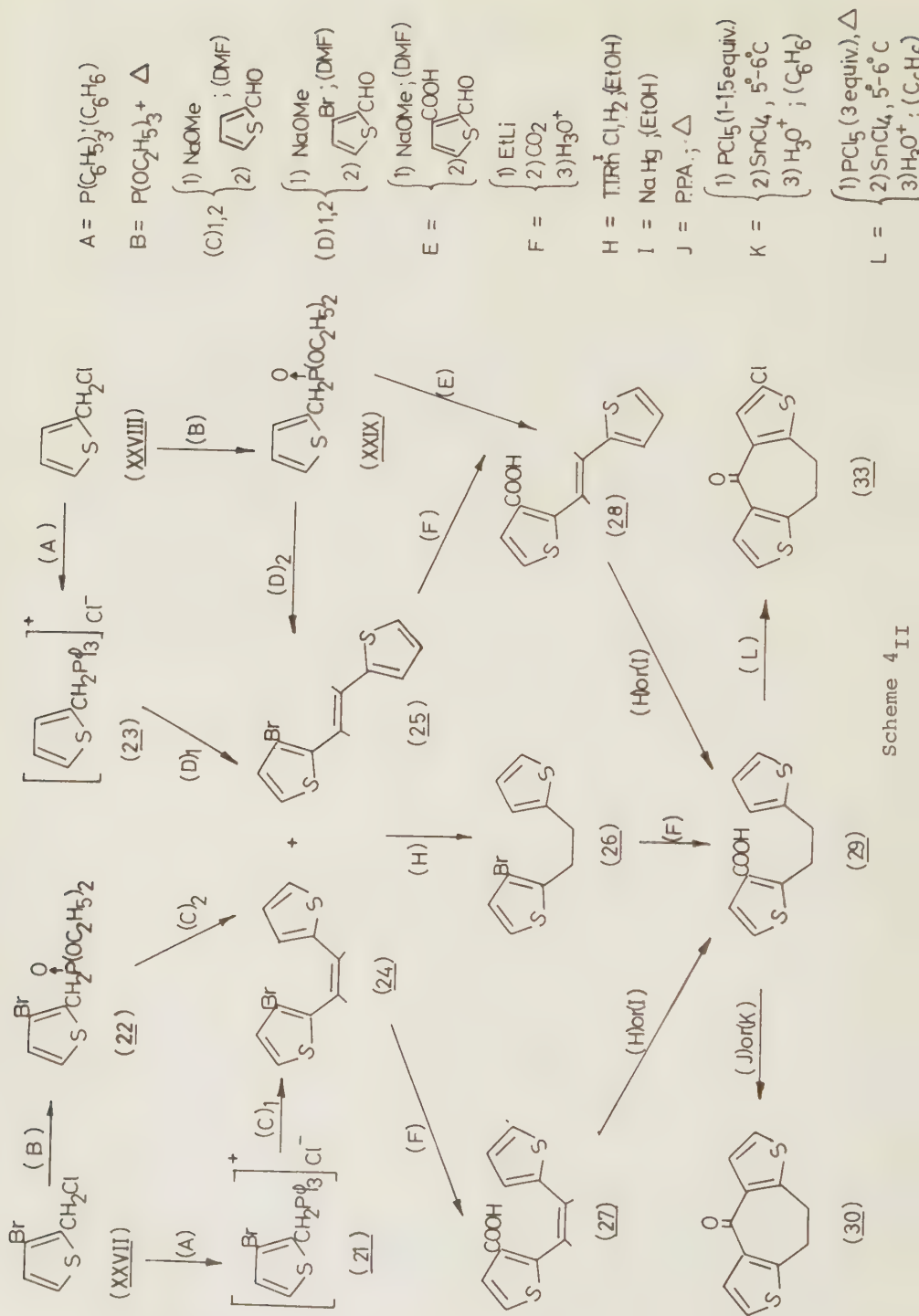


While for (52) a prolonged reflux time in benzene was necessary to obtain the cyclized product (53) (Scheme 6_{II}),

(38) and (50) (Schemes 5_{II} and 6_{II} respectively) failed to cyclize under similar conditions. These observations could perhaps be explained by the -I effect of the chloro substituents for (52) and (38), while a combination of -I and -M effects due to the chloro substituent and the double bond might be responsible for the failure to cyclize in the case of (50).

When the acid (29) was refluxed in benzene 1.5-2 hrs with excess PCl_5 , the acid chloride, which was first formed, underwent electrophilic substitution in the 5-position of the non-carboxylated thiophene ring. Apparently this chlorination is due to the small amounts of chlorine which exist in equilibrium with the PCl_5 in the solution. The POCl_3 which is present in the solution from the acyl chloride formation stage probably acts as Lewis acid for this electrophilic chlorination.

Addition of SnCl_4 to the cooled reaction mixture furnished 2-chloro-8,9-dihydro-4H-cyclohepta[1,2-b;5,4-b']dithiophene-4-one (33) in 82 % yield.



Scheme 4 II

C. Synthesis of 8,9-dihydro-4H-cyclohepta[1,2-c;4,5-c']-
dithiophene-4-one (54)

In preparation of the isomer (54) it was convenient to follow the path already established for the previous systems (13) and (30).

As will be seen in the following discussion, the synthesis of (54) in using this sequence of steps necessitated the synthesis of 1- or 1,3-dichloro derivative of this ketone.

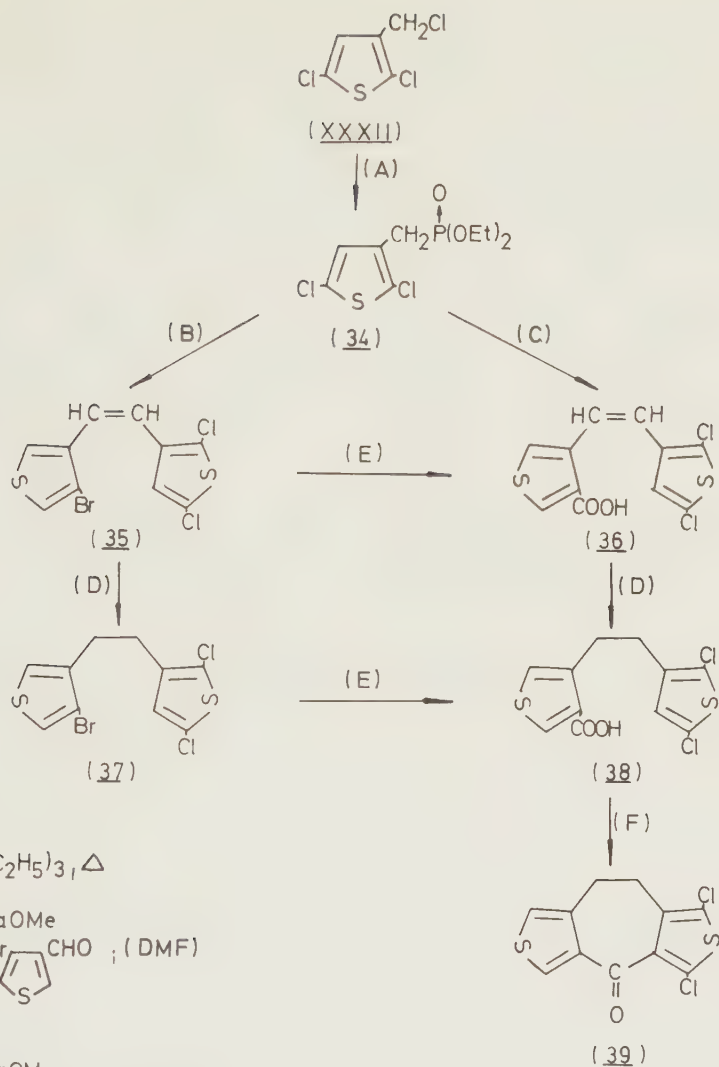
Therefore, the synthesis of the key carboxylic acid 1-(4-carboxy-3-thienyl)-2-(2',5'-dichloro-3-thienyl)ethane (38), according to Reaction Scheme 5_{II}, was undertaken. The blocking of the α -positions of the non-carboxylic thiophene ring of (38) by chloro substituents was necessary in order to direct the electrophilic attack on the 4'-position in the following cyclization step. Otherwise attack would occur on the more reactive α -position instead of the β -position of the non-carboxylic thiophene and this obviously would lead to an undesired isomeric system. It should be emphasized that there is no need to block both α -positions of the non-carboxylic thiophene ring in (38). Indeed, we obtained, as will be described later in this chapter, the monochloro ketone (53), when the 1-(4-carboxy-3-thienyl)-2-(2'-chloro-3'-thienyl)-ethane (52) (see Scheme 6_{II}) was cyclized instead of the dichloro derivative (38). Removal of the chloro substituents from the mono- and disubstituted ketones gave the same product, namely the ketone 8,9-dihydro-4H-cyclohepta[1,2-c;4,5-c']dithiophene-4-one (54).

A summary of the reactions which led to the dichloro-substituted ketone (39) is given in Scheme 5_{II}.

Reaction of the 2,5-dichloro-thienyl chloride (XXXII) (45) by heating it with triethylphosphite afforded diethyl (2,5-dichloro-3-thienyl)phosphonate (34). In the presence of sodium methoxide, (34) reacted with 3-bromo-4-thiophene aldehyde (46)

to give a cis, trans mixture (cis:trans = 50:50) of 1-(4-bromo-3-thienyl)-2-(2',5'-dichloro-3-thienyl)ethylene (35). Homogeneous catalytic hydrogenation of this mixture gave a single saturated product, 1-(4-bromo-3-thienyl)-2-(2',5'-dichloro-3-thienyl)ethane (37). Halogen-metal interconversion of (37) in the usual manner, followed by carbonation, afforded the carboxylic acid 1-(4-carboxy-3-thienyl)-2-(2',5'-dichloro-3-thienyl)ethane (38). In an alternative way (38) was obtained from either reaction of phosphonate (34) with 3-formyl-4-thiophene carboxylic acid (46) followed by homogeneous catalytic hydrogenation of the resulting 1-(4-carboxy-3-thienyl)-2-(2',5'-dichloro-3-thienyl)ethylene (36), or simply by halogen-metal interconversion of the bromo olefin (35) with carbonation in the usual manner, followed by homogeneous catalytic hydrogenation.

Cyclization of the carboxylic acid (38) through its acyl chloride derivative was accomplished by the catalytic action of AlCl_3 , which gave the ketone 1,3-dichloro-8,9-dihydro-4H-cyclohepta[1,2-c;4,5-c']dithiophene-4-one (39) in greater than 70 % yield. Use of SnCl_4 as catalyst instead of AlCl_3 did not afford cyclization even under forcing conditions. The reason, as pointed out previously, probably lies in the -I effect of the two chloro substituents which deactivates the β -thiophene position under attack.



A: $\text{P(OC}_2\text{H}_5)_3, \Delta$

B: $\left\{ \begin{array}{l} 1) \text{ NaOMe} \\ 2) \text{ Br-C}_4\text{H}_3\text{S-CHO} \end{array} \right. ; (\text{DMF})$

C: $\left\{ \begin{array}{l} 1) \text{ NaOMe} \\ 2) \text{ OHC-C}_4\text{H}_3\text{S-COOH} \end{array} \right. ; (\text{DMF})$

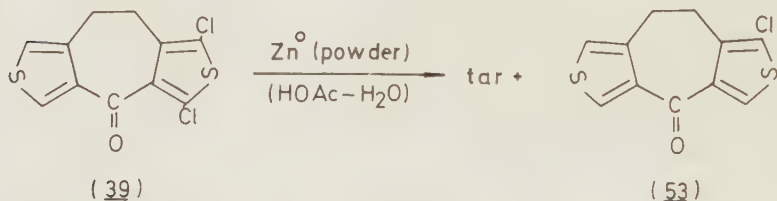
D: $\text{H}_2, \text{T.T. Rh}^{\text{I}} \text{Cl}, (\text{EtOH})$

E: $\left\{ \begin{array}{l} 1) \text{ EtLi} \\ 2) \text{ CO}_2 \\ 3) \text{ H}_3\text{O}^+ \end{array} \right. ; (\text{ether}, -70^\circ)$

F: $\left\{ \begin{array}{l} 1) \text{ PCl}_5 \\ 2) \text{ AlCl}_3 \\ 3) \text{ H}_3\text{O}^+ \end{array} \right. ; (\text{CS}_2)$

Scheme 5_{II}

An attempt to dechlorinate (39) in order to obtain the unsubstituted ketone (54), by the method of MacDowell et al. (47), namely by refluxing (39) in acetic acid - water solution with zinc powder, gave a tar-like product from which only a small amount of the monochloro derivative, (53), could be isolated. The opposing -M effect of the carbonyl and the -I effect of



the chloro substituents ortho to this carbonyl group in (39) make this chloro substituent at 3-position more labile than the other chloro substituent, and thus easier to remove by the action of metals such as zinc or copper in a protic medium. Therefore, it was reasonable to assume that the remaining chloro substituent would be in the 1-position of (53). Support for this conclusion came from the nmr spectrum of this substance in which a doublet at 8.4 ppm ($J = 3.6$ Hz) for H_5 , a singlet for H_3 at 8.2 ppm and a doublet for H_7 at 7.0 ppm ($J = 3.6$ Hz), appeared for the thiophene protons. These assignments are justified, since the deshielding effect of the carbonyl group influences H_3 and H_5 to a greater extent than H_7 , and therefore the former are expected to absorb at lower field than the latter.

The synthesis of 3-chloro-8,9-dihydro-4H-cyclohepta[1,2-c;4,5-c']dithiophene-4-one (53)

An authentic sample of the monochloro ketone (53) which was prepared by the reaction sequence summarized in Scheme 6_{II} was identical to that obtained by reduction of (39).

By carrying out this synthesis we had two objectives in mind: first, to obtain this cyclohepta[1,2-c;4,5-c']dithiophenone system by another sequence of reactions, in which the over all yield, and the reaction conditions were more favorable than they were in the synthesis of (39) in Scheme 5_{II}. Second, we wished to obtain additional information concerning the effect of halo substituents on the stereochemistry of the olefin syntheses under consideration. Here again, the ketone, 1-chloro-8,9-dihydro-4H-cyclohepta[1,2-c;4,5-c']dithiophene-4-one (53), could be obtained from the carboxylic acid 1-(4-carboxyl-3-thienyl)-2-(2'-chloro-3'-thienyl)ethane (52), by converting it in situ to the acyl chloride derivative, followed by ring closure with SnCl₄ as acid catalyst.

Much more vigorous reaction conditions in terms of prolonged reaction time and higher temperature were necessary compared to cyclizations of (12), (19) and (29) (see Schemes 2_{II}, 3_{II} and 4_{II}, respectively).

The carboxylic acid (52) was obtained from cis and/or trans 1-(4-bromo-3-thienyl)-2-(2'-chloro-3'-thienyl)ethylene (47) and/or (48) in the following way. Lithiation followed by carbonation of the isomeric bromides gave the unsaturated carboxylic acids cis and/or trans 1-(4-carboxy-3-thienyl)-2-(2'-chloro-3'-thienyl)ethylene (50) and/or (51), which on subsequent hydrogenation furnished the desired product (52).

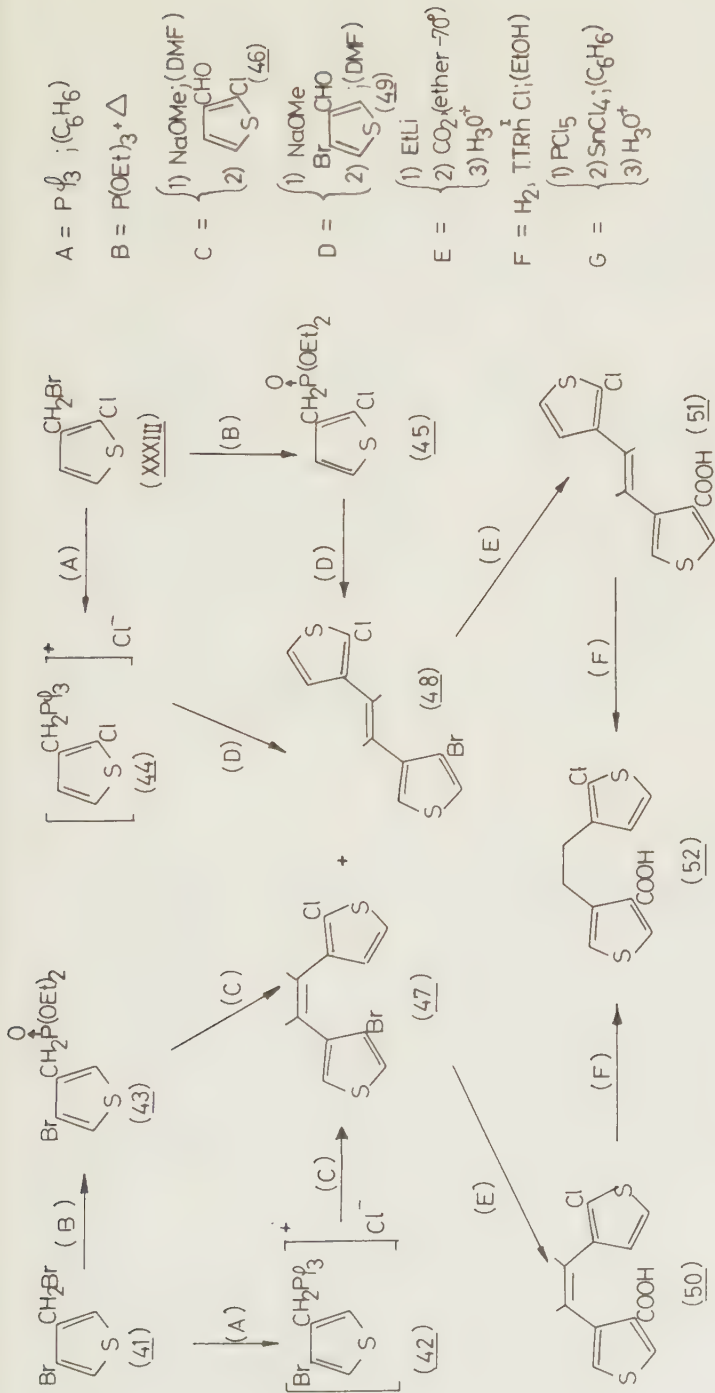
The saturation of the olefinic double bonds in (50) and/or (51) could be accomplished reasonably fast regardless of whether the compound was cis or trans or a mixture of isomers by the homogeneous catalytic hydrogenation method (40).

The cis-trans isomer distribution, in four modified paths of olefin synthesis, by which we obtained (47), (48), followed the same general tendencies as already observed in the other olefin syntheses in this work. When the phosphonium salts 3-bromo-4-thienyltriphenylphosphonium bromide (42) and 2-chloro-3-thienyltriphenylphosphonium bromide (44) were reacted with the appropriate halogen substituted thiophene aldehydes, the cis olefin (47) was obtained in larger amount than the trans isomer (48). On the other hand, although reactions of diethyl-(3-bromo-4-thienyl)phosphonate (43) and diethyl-2-chloro-3-thienyl-

phosphonate (45) with 2-chloro-3-thenaldehyde (46) (48) and 3-bromo-4-thenaldehyde (49), respectively, gave larger amounts of trans isomer (48) than cis (47) as expected, the amount of cis in this reaction was unprecedentedly high among the reported phosphonate-olefinations. As we have seen, similar behavior was observed in the synthesis of olefin (35) in Scheme 5_{II}. The stereochemistry of these phosphonate olefinations is discussed in Chapter III.

The phosphonium salts (42) and (44) were prepared by the reactions of 3-bromo-4-thenylbromide (41) and 2-chloro-3-thenylbromide (XXXIII) (48) with triphenylphosphine in benzene. The phosphonates (43) and (45) were obtained when (41) and (XXXIII) were heated with triethylphosphite.

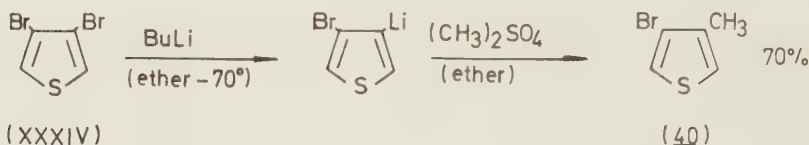
The compound (41) was obtained from side-chain bromination of 3-bromo-4-methylthiophene (40) by NBS in a modification of the method of Gronowitz et al. (50) using ABN as the radical initiator.



Scheme 6 II

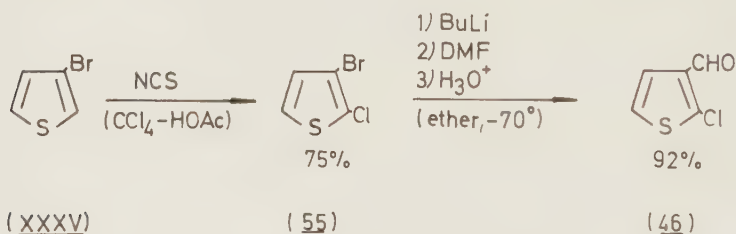
A new route for the synthesis of (40) has been introduced here, which besides giving an overall higher yield than in a previous method (50) was also more convenient and less time-consuming.

In this method, 3-bromo-4-thienyllithium, which was obtained from halogen-metal interconversion of 3,4-dibromothiophene (XXXIV) at -70° , was reacted with dimethylsulphate and gave (40) in about 70 % yield.



The 2-chloro-3-thiophene aldehyde (46) which was prepared by Campaigne and coworkers (48), could be prepared in a simpler method with much higher yield.

3-Bromothiophene was chlorinated with one equivalent of NCS in $\text{HOAc}-\text{CCl}_4$ solution (1:1), and the 2-chloro-3-bromothiophene (55), which was obtained in 75 % yield, was treated with one equivalent of BuLi at -70° followed by addition of dry DMF. Subsequent hydrolysis of the reaction mixture afforded the aldehyde (46) in 92 % yield.



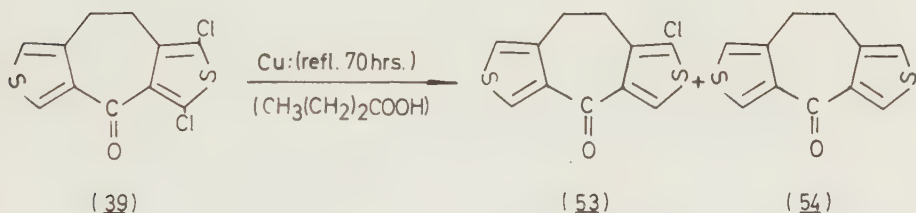
phene (55), which was obtained in 75 % yield, was treated with one equivalent of BuLi at -70° followed by addition of dry DMF. Subsequent hydrolysis of the reaction mixture afforded the aldehyde (46) in 92 % yield.

Dehalogenation of (39) and (53)

As mentioned previously, an attempted dechlorination of (39) by zinc in acetic acid produced only small amounts of monochloro derivative (53), and use of zinc appeared to be destructive for this ketonic system.

A modification of this method, which was first introduced by Gol'dfarb et al. (87) and which makes use of copper in propionic acid for dehalogenation of α -thiophenes, gave much better results in this case.

The ketone 8,9-dihydro-4H-cyclohepta[1,2-c;4,5-c']dithiophene-4-one (54) was obtained in 71 % yield when its dichloro derivative (39) was boiled in butyric acid for 70 hrs. The unsubstituted ketone (54) was separated from the monochloride (53) by fractional crystallization in acetonitrile. The residue



after concentration of the mother liquor consisted of (53) and (54), and could be refluxed for further dechlorination.

The great advantage of the copper modification over the zinc method lies in the high recovery of the ketonic system in the former compared to the destructive nature of the latter.

The Wittig and Wadsworth-Horner syntheses of some dithienylethylenes

A. General synthetic conditions

Early in the program, it was realized that a *cis* stereoselective synthesis of certain dithienylethylenes would be of considerable synthetic value, since it would save two steps in the overall synthesis of the dithienotropylium ions. Our initial successes along these lines prompted a more thorough investigation of the factors governing this stereoselective synthesis.

For this purpose, all the olefination reactions performed in the course of the dihydrocycloheptadithiophene-one syntheses (Chapter II) were completed along with a few others. The results of these olefin syntheses are the subject of this chapter.

All the Wittig olefin syntheses in which phosphonium bromides or chlorides were involved were carried out by first forming the corresponding phosphorane *in situ* followed by addition of the desired aldehyde.

Olefinations in which phosphonates were involved were carried out by dropwise addition of a solution of phosphonate and aldehyde to the suspension of base. The solvent used in these syntheses was DMF, which was dried by refluxing over, followed by distillation from calcium hydride. The base used was commercial sodium methoxide.

These reactions were often exothermic, and appeared to be rapid, as evidenced by the instantaneous disappearance of the color of the phosphoranes upon addition of aldehyde. The exothermicity of both phosphorane and phosphonate ylid olefinations

were indicative in this respect also. Reaction temperatures were usually kept somewhat under room temperature during the addition of aldehyde.

Triphenylphosphine oxide, the by-product from the Wittig reaction, was easily separated by elution of the crude reaction product on a column of silica gel with benzene (52).

B. General physical properties of the 1,2-dithienylethylenes

The cis isomers of these systems had consistently lower melting and boiling points than their trans isomers. While the trans isomers could be easily obtained pure, by fractional precipitation from solvents, this was not possible in the case of the cis isomers, which had higher solubility. Trituration of the mixture with hexane in order to extract the cis isomer selectivity, also did not give satisfactory results. Attempts to separate the isomers by vacuum distillation were also unsuccessful. The cis-enriched fraction of the monobromide, however, could be converted into their carboxyl derivatives, the cis isomer of which could be separated in the pure state by trituration under hexane.

Distinctions between the cis and trans isomers could be made as follows:

a) The nmr spectra of the trans isomers in general, and their olefinic protons particularly, exhibited a downfield shift when compared to those of the corresponding cis isomers.

This downfield shift effect can be attributed to the more effective conjugation in the trans form than in the corresponding cis isomer.

b) The facts that physical properties such as melting and boiling points are often higher for trans than for cis isomers, and that usually a much larger amount of trans isomer than cis isomer is obtained in phosphonate olefinations (39,72), were used for structural assignments.

c) The carboxylic acid derivatives assigned the cis configuration cyclized to give the expected cycloheptadithiophene-ones, whereas those assigned the trans configuration did not undergo cyclization.

The cis:trans ratios, given in Tables 1_{III} and 2_{III}, were determined by glc analyses of the crude reaction mixtures, after $\phi_3P=O$ was removed, using a 10 % BDS on Chromosorb W column at column temperature of 210-215°. The trans isomers without exception had longer retention times than their cis counterparts.

C. Mechanism and stereochemistry

1. General observations

Already with the first Wittig olefin syntheses of the bromo-1,2-dithienylethylenes, it had been noticed that this group of reactions might have, besides their immediate synthetic utility, some other interesting features, which would make a more detailed investigation worthwhile.

From this point of view, all the Wittig and Wadsworth-Horner syntheses of halosubstituted 1,2-dithienylethylenes, already mentioned in Chapter II, and their results are collected in Tables 1_{III} and 2_{III}. To complete the general picture obtained from these observations, a few other olefination reactions were performed which were also added to these tables.

Although this is by no means a complete or comprehensive investigation, some general stereochemical trends can be observed. Some of these trends have been already mentioned elsewhere, but will be repeated here for the sake of completeness:

- 1) A high proportion of cis isomers was often obtained in Wittig olefinations (Table 1_{III}).
- 2) While introduction of a bromo substituent on the thiophene nucleus of the thenylidene phosphoranes in these Wittig reactions had a small influence on the stereochemistry of the products, a halo substituent on the reacting thenaldehyde altered the proportion of isomers drastically in favour of the cis isomer.
- 3) Additives such as lithium iodide in the reaction mixture, which has been reported (55) to have a strong influence on the stereochemistry of Wittig reactions in some cases, did not show any observable effect on the stereochemistry of these thenylidene phosphorane olefinations.

4) The stereochemistry of the phosphonate olefinations (Table 2_{III}) was sensitive to a halogen substituent either in the aldehyde or the thenyl moiety of the phosphonate. A halogen substituent on either of them increased the cis ratio in the products. Furthermore, this effect seemed to be additive, in the cases where both aldehyde and phosphonate were substituted. Extraordinarily high ratios of cis olefins (up to 50 %) have been observed in olefinations of chloro-substituted thenyl-phosphonates.

2. Theory of stereochemistry of Wittig olefin syntheses

For an interpretation of these results a theoretical perspective of phosphorylidene-carbonyl olefin synthesis is necessary. In the following few pages, some of the theoretical aspects of these olefin syntheses will be reviewed, and understandably, attention will mainly be focused on the stereochemistry of these reactions.

The nature of the phosphorane. Already in their classical paper "Uber Triphenylphosphinmethylen als olefinbildende Reagenzien" Wittig and Schölkopf (53) mentioned the fact that the reaction between α -monosubstituted phosphorous methylides and aldehydes afforded equal amounts of cis and trans olefins. Since this finding was according to the expectations, this reaction seemed to offer no stereochemical problems. Bohlmann et al. (54) were the first to observe preferential yields of the thermodynamically less probable cis olefins in some cases, and later on Shemyakin and co-workers (55,56,57) investigated the cis selectivity systematically.

Trans stereoselectivity was reported some few years later by House and Rasmusson (58), and was found to be a general characteristic of the Wittig reaction whenever so-called "stable" ylids are involved.

It is a matter of convenience to distinguish between the two extreme groups of phosphorane ylids (59,60), namely the resonance stabilized (XXXVI) and the reactive (XXXVII) alkylidene phosphoranes.



R = alkyl, aryl

(XXXVI): $R' = -CN, -COOR'', -COR''$

(XXXVII): $R' = \text{alkyl}$

(XXXVIII): $R' = \text{aryl, thienyl, } -CH=CH-, -C\equiv C-$

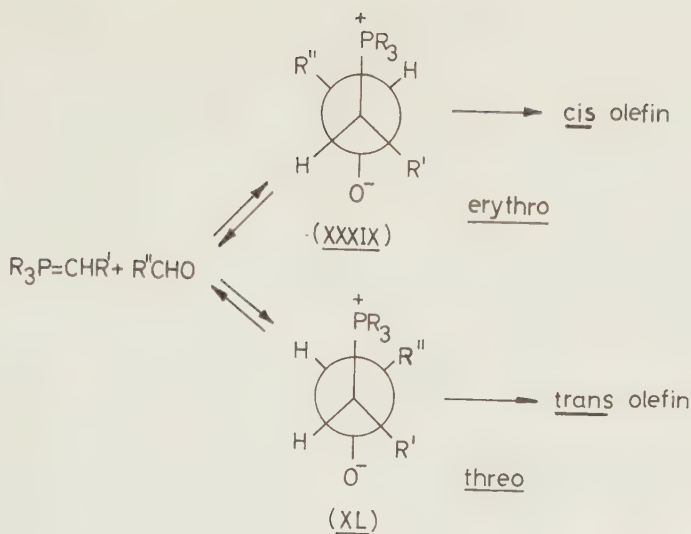
In the series (XXXVI), the cyano, carbalkoxy and acyl groups stabilize the ylid function through inductive and mesomeric effects. As a result these phosphoranes are quite stable to hydrolysis and, in fact, are formed from the corresponding phosphonium salts in aqueous alkaline media. On the other hand, the phosphorane ylids (XXXVII) in which the carbanion has little or no stabilization through either inductive or mesomeric effects, are highly reactive. This is exemplified by the fact that strong bases are needed to generate them from the phosphonium precursors.

In between these two extremes fall phosphoranes, (XXXVIII), which are stabilized to some extent through conjugation to an aromatic ring or other conjugated system.

The degree to which the phosphorane ylids are stabilized is one of the important factors determining the over-all stereochemistry of the reaction, but not the only one.

It is well established that the Wittig reaction proceeds in two steps (59,60,61). First a reversible formation of an open-chain zwitterionic betaine, which then decomposes via its cyclic oxaphosphetane (62) form to olefin through cis elimination of triphenylphosphine oxide.

In salt-free solutions, the betaine intermediate normally tends to form the erythro configuration, (XXXIX), rather than threo (XL) (60). Therefore, if the betaine formation step is irreversible, the cis olefin would largely predominate in the products.



For highly reactive phosphoranes (XXXVII), the process of betaine formation is practically irreversible, and therefore a high proportion of the cis isomer is to be expected. This is provided, however, that the activation energy of the betaine decomposition to products is not too high relative to that of the betaine formation step. In short, one can say that, in this particular case, it is the kinetically controlled betaine formation step which determined the cis stereoselectivity of the reaction, and the betaine decomposition step has little or no significance for the final isomer composition.

In cases when resonance stabilized phosphoranes (XXXVI) are employed, the betaine formation step will be reversible (63), and therefore, the steric factors leading to the energy differences between the two epimeric betaines are of importance in the transition state. In other words, this will be a thermodynamically controlled process, in which the rate of formation of the more stable threo epimer may equal or exceed the rate

of erythro formation. In such a case, the degree of stereospecificity of the reaction will be dependent largely upon the relative decomposition rates of the epimeric betaines to products.

The trans stereoselectivity which is so often associated with stable phosphoranes, can be further enhanced through more effective conjugation, as well as the absence of steric crowding in the threo $\rightarrow$ trans transition state as compared to the transition state of the erythro $\rightarrow$ cis process. As a consequence, the threo epimer collapses to products at a higher rate than the erythro and thus will be replenished by the equilibrium, through which both diastereoisomeric betaines can be rapidly interconverted.

The role of the carbonyl compound. Up to now, the role of the carbonyl compound has not been considered as a factor in the determination of stereochemistry of phosphorane olefinations. The reason for this neglect was that we have so far been dealing with extreme cases of "reactive" and "stable" phosphoranes in which the nature of the carbonyl compound was not supposed to have a marked effect on the energy profiles of the individual steps. It should, however, be emphasized that it is mainly for the sake of clarity, which made many authors resort to these extreme cases as models, in order to discuss the stereochemistry of the Wittig reaction.

In between these two groups of extreme phosphoranes, there exists a large number of mildly reactive phosphoranes, in which the α -carbanion is conjugated to an aromatic ring system, or an isolated double or triple bond (XXXVIII). It is with these phosphoranes that the nature of the carbonyl group may have a great influence on the stereochemistry of the olefin. Since the delocalization of the negative charge in these phosphorane is not as effective as in the (XXXVI) derivatives, olefinations effected with these moderately reactive ylids are usually devoid of marked stereospecificity (64) (triphenylbenzylidene phosphorane is one example of this sort). Although factors governing the stereochemical course are the same for the moderate as well as the extreme cases of phosphoranes, in the former case, a rather delicate balance between the rate constants

of the betaine formation and betaine decomposition will determine the cis:trans ratio of the products. Such a balance, which is a result of the combination of different effects, will be susceptible to small energy variations which are caused by small electronic or steric changes in the intermediates. Because of the intermediary nature of these phosphoranes, which means low activation energies in betaine formation and betaine decomposition steps, such small energy variations in the reaction may cause appreciable changes in the balance of rate constants, and alter the isomer distribution markedly in the reaction.

As in the case of stable phosphoranes, the intermediate betaines could not be isolated (61), and hence transition states both of betaine formation and betaine decomposition, in accord with Hammond's hypothesis (65), are much closer in character to the betaine than to reactants or products respectively. A reasonable conclusion will be therefore that conjugation factors in the products will not be well developed in the transition state leading to it. Therefore, other factors being equal, both enantiomers will collapse to product at similar rates. In such a case, the final isomer distribution will be determined by the first step, namely the betaine formation, where the formation step in which electronic factors, inductive and/or mesomeric effects, of the reactants are of major importance. In other words, for moderated phosphoranes this step is anomalous in nature, standing midway between thermodynamic and kinetic control, and rather small electronic changes in the phosphorane or the carbonyl compound may bring about an appreciable change in the ratio of betaine enantiomers, which will be accordingly reflected in the isomer ratio of the olefin.

It has been found for instance (66,67) that electron-donating substituents, which enhance the nucleophilicity of the ylid, reduce the amount of trans isomer formed, while electron-withdrawing ligands increase it. The cis stereoselectivity of triphenylphosphonium propynylid (68) indicates that mesomeric stabilization is less effective for this phosphorane than for triphenylphosphonium allylid (53,69) in which the trans isomer is slightly predominant.

Also reactivity changes in the carbonyl group, caused by electronic effects, may markedly affect the stereochemical outcome in reaction with a moderated phosphorane. This again is consistent with the anomalous nature of these phosphoranes. When such a phosphorane reacts with a highly reactive aldehyde, the reversible decomposition of the reaction intermediates may be out-run by the triphenylphosphine oxide elimination, and an essentially kinetically-controlled reaction will prevail, and thus a high ratio of cis olefin will be expected.

Although steric factors may influence the rates of betaine formation of a moderated phosphorane, their major contribution will be rate enhancement of the cis product due to steric relief, which is greater for the erythro $\rightarrow$ cis transition state than for threo $\rightarrow$ trans.

D. Interpretation of the results obtained in phosphorane olefinations

In the light of the foregoing discussion, we are now ready to examine in detail and rationalize the results of the thenylidenephosphorane olefinations with thiophene aldehydes.

These results are collected in Table 1_{III} where the reported cis, trans ratios were determined by a glc method (see details in Chapter VI, Section C, No 1). The values for these ratios are an average of three determinations.

All these reactions were carried out under the same reaction conditions, according to general procedure No 1, Section C in Chapter VI.

Examination of Table 1_{III} reveals the following stereochemical trends.

- 1) The reactions of unsubstituted thenylidene phosphoranes and thiophene aldehydes do not exhibit marked stereoselectivity. This is evident from an examination of the product ratios in reactions 1, 2, 7 and 8, in which the phosphoranes used are of the same order of nucleophilicity.

2) Introduction of a bromine atom ortho to the ylid function introduces some stereoselectivity when compared with the non-substituted phosphoranes. Comparison of reactions 3 and 9 reflects the balance between the +M and -I effects of the bromine in phosphoranes (62) and (64) respectively.

Assuming equal -I effect for bromine in either the 2- or the 3-position of the thiophene ring, then the trans stereoselectivity shift which occurs in reaction 9 can be rationalized in terms of a weak mesomeric (+M) effect along with a stronger inductive (-I) effect of the β -bromosubstituent in (64). This results in a net electron-attraction from the system and hence results in a stabilization of the carbanion.

In (62), both the -I and +M effects of the α -bromo substituent may nearly balance each other. This fact, along with the less effective conjugation of the phosphorane carbanion with the system through the β -position, may explain why the stereochemistry in reaction 3 is not affected or even slightly cis stereoselective compared to that in reaction 1.

3) Introduction of a bromine atom ortho to the aldehyde function gives a marked increase in cis stereoselectivity (see reactions 5 and 10). This is due to the increased electrophilicity of the carbonyl carbon atom caused by the -I effect of the ortho bromine. The increase in the betaine formation rate, caused by this electronic effect, renders the reaction kinetically controlled and hence cis stereoselective. That steric factors are not involved in these reactions, can be easily seen from the results of reaction 13.

4) The high cis stereoselectivity in reactions 6, 12, 14, 15 and 16, is obviously due to the combined effects of the halogen substituents both on the phosphoranes and the aldehydes. Therefore the cis stereoselectivity in these reactions is not surprising. On the other hand, in contrast to reactions 5 and 10, steric factors may not be completely excluded from determining the extent of the cis stereoselectivity in these reactions.

This statement is supported by examination of reaction 12. If one assumes that the electronic effects of phosphorane (64) and 3-bromo-2-thiophenealdehyde are opposing factors in the stereochemistry of this reaction, as described for reactions 9

and 10, then the amount of cis product in 12 should decrease compared to that in 10. Furthermore, the bulky ortho bromo substituents in the reactants, can only serve to slow down the betaine formation step and give increased chance for equilibration of the two epimers, which means a decrease in the amount of erythro form, and consequently, further decrease in the amount of cis isomer. However, the slightly larger amount of cis product in 12 than in 10 points to a factor of steric relief in the transition states of the decomposition step of the epimers to products, which is greater for the erythro $\rightarrow$ cis decomposition. In principle, similar arguments may explain the high cis stereoselectivity in reactions 6, 14, 15 and 16. But application of such arguments to these particular cases will not be as easy as for 12. This is because the different effects superimpose in such a way that distinction between them is made very difficult, and perhaps additional experimental data are needed.

The term "moderated" which has been used to characterize the behavior of thenylidenephosphoranes in this discussion should not be taken in its strict sense, but more in terms of relatively equal energy barriers for the two steps; reactants $\rightarrow$ betaine $\rightarrow$ products, and also intermediate betaines which are rather unstable.

Judging from the rapid reactions with the thiophene aldehydes at low temperatures and from the fact that most of the olefin was formed during the first few minutes in these reactions, thenylidenephosphoranes, in fact, are highly reactive intermediates.

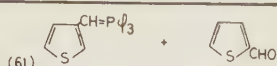
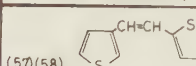
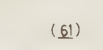
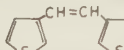
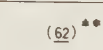
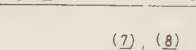
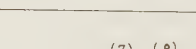
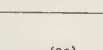
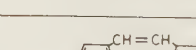
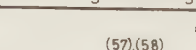
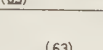
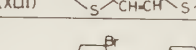
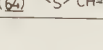
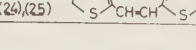
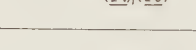
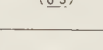
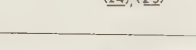
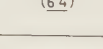
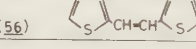
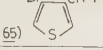
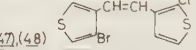
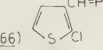
The ease with which these phosphoranes underwent intermolecular C-alkylations is demonstrative for this reactivity.

Triphenyl-2-bromo-3-thenylidenephosphorane (62) and triphenyl-3-bromo-4-thenylidenephosphorane (65) were reacted in DMF, with 2-bromo-3-thenylbromide (XXIII) and 3-bromo-4-thenylbromide (41) to give the phosphonium salts (67) and (69) respectively (Schemes 1_{III} and 2_{III}). The salts (67) and (69) were treated in situ each with a portion of sodium methoxide. The resulting phosphoranes (68) and (70) afforded upon further treatment with water the compounds sym-di(2-bromo-3-thienyl)ethane (3) and sym-di(4-bromo-3-thienyl)ethane (71)

respectively in yields of 40-42 %.

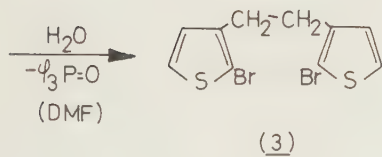
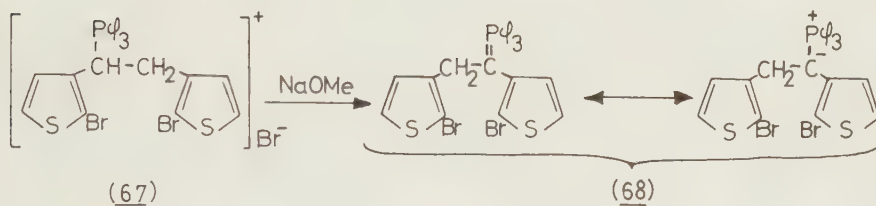
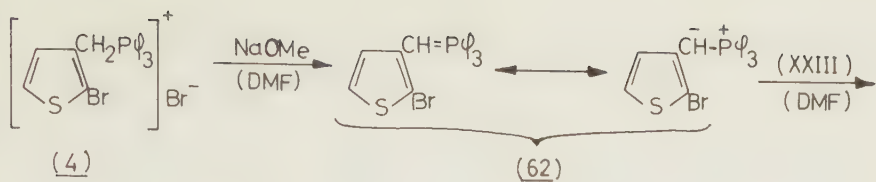
Intramolecular C-alkylations of reactive phosphoranes were carried out previously by Bestmann et al. (71), but no intermolecular alkylation has been reported so far.

Table 1_{III} Results of reaction of some triphenylthienylidene-phosphoranes with some thiophenealdehydes

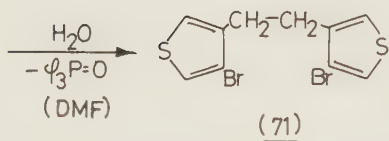
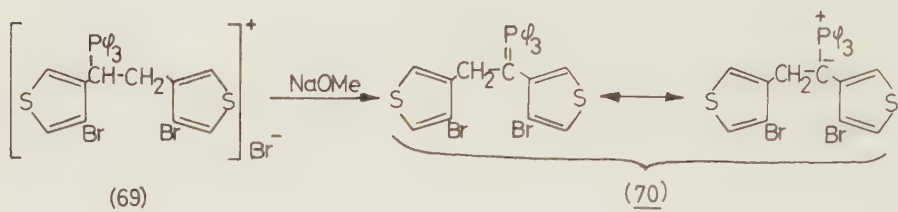
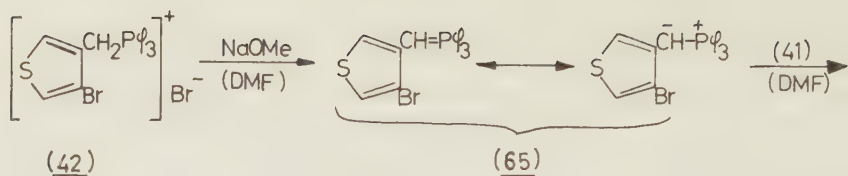
React.		Reactants in DMF	Olefin products (cis) (trans)		Yield %	cis:trans ratio
ser.	no.					
A	1	 + 		*	—	49:51
	2	 + 	 (85)	(XLI)	—	52:48
	3	 + 		(7), (8)	76	56:44
	4	 + 		(7), (8)	52	52:48
	5	 + 		(2), (8)	72	70:30
	6	 + 	 (52)	(XLIII)	—	74:26
B	7	 + 		*	—	56:44
	8	 + 	 (85)	(XLII)	—	48:52
	9	 + 		(24)/(25)	69	37:63
	10	 + 		(24), (25)	83	70:30
	11	 + 		(24), (25)	75	72:28
	12	 + 		(56)	70	75:25
	13	 + 		(59)(60)	—	55:45
C	14	 + 		(47), (48)	76	73:27
	15	 + 		(47), (48)	75	75:25
	16	 + 		(XLIV)	—	81:19

* The products were not isolated.

** Lithium iodide was added to the phosphorane.



Scheme 1_{III}



Scheme 2_{III}

E. Stereochemistry in olefination - Reactions of the diethyl thenylphosphonate ylids

It seems to be somewhat more difficult to explain the isomer distribution which resulted from the series of olefinations involving the diethyl-thenylphosphonate carbanions, which are summarized in Table 2_{III}. The difficulty lies mainly in the fact that this modification of carbonyl olefinations has been little studied.

Theoretical background. Two main features of the phosphonate modification of olefin syntheses have been already established: First, the product forming step, which is slow, in contrast to the rapid reaction of the phosphonate ylids with aldehydes, can in general be brought about only when the intermediate is activated at the position α - to the phosphorus. Therefore, the phosphonate modification is limited mainly to the synthesis of conjugated ethylenes (72,73).

Second, as there is a low barrier for betaine formation and a high barrier separating the intermediate betaines from the products, diastereoisomeric equilibration will prevail and consequently trans stereoselectivity should, as a rule, be a characteristic feature of phosphonate carbonyl olefination. Indeed, this has been the case in all carbonyl olefinations investigated so far: the trans isomer formed more than 90 % (39) of the olefinic product.

Nevertheless, the possibility of reduced trans stereoselectivity or even lack of it cannot be ruled out completely.

Interpretation of the results. In Table 2_{III}, results of a series of olefinations involving diethyl-thenylphosphonate ylids are recorded. Some surprisingly high cis proportions have been observed for some of these reactions. An attempt will be made here to rationalize these results in accordance with the foregoing discussion.

As these ylids are very reactive nucleophiles in olefination with an aldehyde, they tend to produce an initial preponderance of the erythro betaine (kinetically controlled step).

Here again as, in the case of phosphorane olefinations with larger groups in the reactants, an increased proportion of cis olefin in the products can be realized (39), which as previously stated is attributed to the greater steric relief of erythro decomposition to product.

It has been already stated that the PO betaine, as we may call the intermediate betaines of phosphonates, may collapse to olefin and phosphate only if there is activation of the atom α to phosphorus. This activation assists the process of bond-dissociation, bond-formation, in the four-membered transition state, by dispersion of partial negative charge at the α -position, through mesomeric or inductive effects of the group attached to this position. This in turn causes a lowering of the energy barrier for the betaine decomposition step which means not only an over all higher reaction rate, but also an increased probability of erythro betaine decomposition to cis olefin. Therefore, the more α -activated PO betaines will be less trans stereoselective in carbonyl olefinations.

The nature of the carbonyl compounds. Finally we should consider the role of the carbonyl group in the stereochemistry. Somewhat similar reasoning to that presented in the case of the phosphoranes, may be also valid for α -activated PO ylids. Namely, a reactive aldehyde (more electrophilic carbonyl carbon) enhances the tendency of erythro betaine formation. If the betaine decomposition steps to products are unaffected, then an increase in cis production would be the consequence.

Discussion of the results. In applying the foregoing hypotheses to the results of the phosphonate olefin syntheses in Table 2_{III}, these observations can be rationalized.

1) In all three series a, b and c, bromo substitution ortho to the ylid function of the thenylphosphonates decreases the trans stereoselectivity of the reaction when compared to an unsubstituted thenylphosphonate. This can be attributed to the -I effect of the halogen, which increases the decomposition rate of the

betaine to products through α -activation in the transition state.

2) The general tendency of the 2-thenyl phosphonates to produce more cis isomer than the 3-substituted isomers (compare series a and b in Table 2_{III}) can be ascribed to the more effective α -activation of the betaines in the transition state of the decomposition step by the 2-thenyl moiety than by the 3-thenyl moiety, due to the better conjugative properties of the former (28). This enhances the betaine decomposition rate and hence cis production.

3) The ortho halothiophene aldehydes produce more cis olefin than unsubstituted thiophene aldehyde. This can be seen when reactions 1 and 6 are compared to 3 and 8 respectively. These halothiophene aldehydes are considered better electrophiles than the unsubstituted ones, and therefore the arguments in the theoretical background, concerning increased cis production due to the more reactive carbonyl groups, may be applied here.

Also, assuming that phosphonates (73) and (77) are of similar reactivity this effect can be seen clearly by comparison of the percentages of cis isomer in reactions 4 and 10.

4) The effect of nuclear chloro substitution on the stereochemistry of the thenylphosphonate olefinations is drastic and is well-demonstrated in reactions 11 and 12.

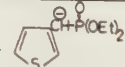
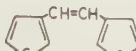
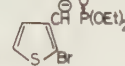
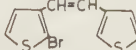
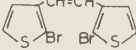
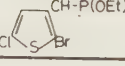
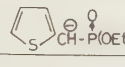
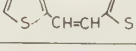
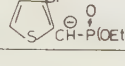
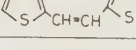
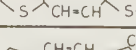
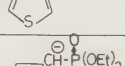
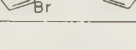
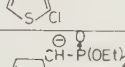
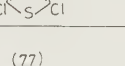
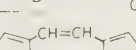
Phosphonate ylids (78) and (79), in reaction with 4-bromo-3-thiophene aldehyde, furnished the hitherto unprecedentedly high cis proportions 33 % and 50 % respectively.

The chloro substituents in these phosphonates cause an appreciable rate increase of the second step through α -activation in the transition state.

It can be concluded, in comparing reactions 11 and 12, that the nuclear chloro substituent in thenyl phosphonates affects the stereochemistry of the olefination only inductively. Since if it were mesomeric, the 5-chloro substituent in (79) would not be able to alter the cis, trans ratio which was obtained for (78) in reaction 11.

To conclude this chapter, it should perhaps be added that the interpretations which were presented here in order to explain the observed isomer distribution for both phosphorane in Table 1_{III} and phosphonate, in Table 2_{III} olefin syntheses are of a more suggestive nature, which may serve as a guide-line for a more systematic investigation of these ylids.

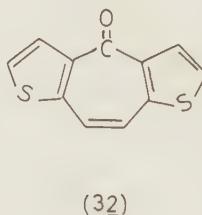
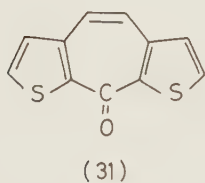
Table 2_{III} Results of some diethylthienylphosphonate olefinations with some thiophenealdehydes

React. ser. no.	Reactants in DMF	Olefin products (cis) (trans)	Yield %	cis:trans ratio
A	1 (72)  + 	(XLI)  (85)	—	3:97
	2 (73)  + 	(2), (8) 	92	5:95
	3 (72) + 	(7), (8)	90	8:92
	4 (73) + 	(XLIII)  (53)	—	10:90
	5 (74)  + 	(12) 	86	—
B	6 (75)  + 	(XLI)  (85)	—	3:97
	7 (76)  + 	(24), (25) 	95	8:92
	8 (75) + 	(24), (25)	93	10:90
	9 (76) + 	(56)  (32)	—	13:87
C	10 (77)  + 	(47), (48) 	94	17:83
	11 (78)  + 	(47) (48)	92	33:67
	12 (79)  + 	(35) 	85	50:50
	13 (72) + 	(XLIV)  (33)	—	13:87

Di thienotropylium ions

Part 1. Synthetic methods

The ketones 9H-cyclohepta[2,1-b;4,5-b']dithiophene-9-one (31) and 4H-cyclohepta[1,2-b;5,4-b']dithiophene-4-one (32)

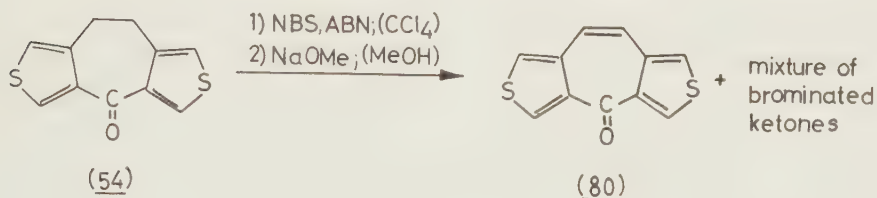


were previously obtained (see Chapter II) by cyclization of the corresponding *cis* carboxylic acids. Alternatively, they were obtained in good yield (85-90 %) through side-chain bromination, dehydrobromination of the corresponding dihydro precursors (13) and (30).

Each of these alternative methods possessed certain advantages. While cyclization of the *cis* carboxylic acid reduces the synthetic sequence by three steps, the bromination-dehydrobromination method furnished overall higher yields of the final products with experimentally simpler procedures. In the latter method, *trans* olefins could be used as well as *cis*, which eliminated cumbersome *cis-trans* separation process for the olefins, obtained from Wittig reactions (Schemes 2_{II} and 4_{II}). In addition, the inconvenient phosphonium method of

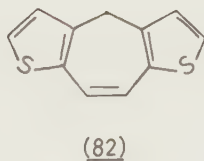
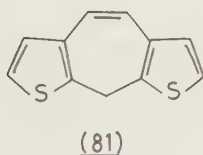
olefination could be substituted by the simpler phosphonate method, which also afforded considerably higher yields of olefin.

This matter of choice did not exist for the third isomeric ketone 4H-cyclohepta[1,2-c;4,5-c']dithiophene-4-one (80), because any attempt to obtain it by cyclization of the corresponding cis carboxylic acid would probably lead to an undesired isomer. Therefore, (80) was obtained through the bromination-dehydrobromination of the dihydro precursor (54) in 70 % yield.



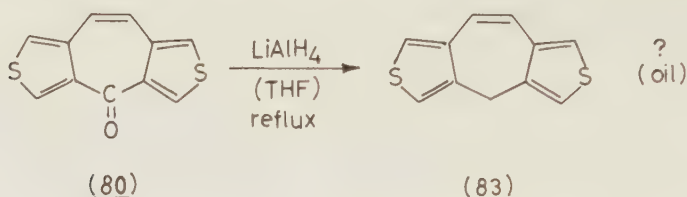
The carbonyl functional groups in these cycloheptadithiophene-ones were reduced readily to the corresponding methylenes by LiAlH_4 in ether solution. No Lewis acids such as AlCl_3 were required. This is undoubtedly due to the strongly polarized character of the C-O bonds. This aspect will be discussed later in more detail.

The hydrocarbons 9H-cyclohepta[2,1-b;4,5-b']dithiophene (81) and 4H-cyclohepta[1,2-b;5,4-b']dithiophene (82) were obtained



in nearly quantitative yields by LiAlH_4 -reduction of the corresponding ketones (31) and (32) in ether solution. Reduction of the third isomer, namely the C-annulated cycloheptadithiophene-one (80), was carried out also by LiAlH_4 in THF solution. The presence of 4H-cyclohepta[1,2-c;4,5-c']dithiophene (83) hydrocarbon could not be fully established so far, and the only

evidence that we have used to assume its formation in the reaction was derived from the MS of the tan oily product, and



also from the fact that no characteristic OH-stretching band was observed for the product while the C=O-stretching band disappeared completely.

Dauben et al. (74) prepared a number of tropylium salts through hydride exchange reactions between cycloheptatrienes and trityl perchlorates in polar solvents. We found this method very efficient for obtaining the dithienotropylium perchlorates from the corresponding cycloheptadithiophene (Fig 1_{IV}).

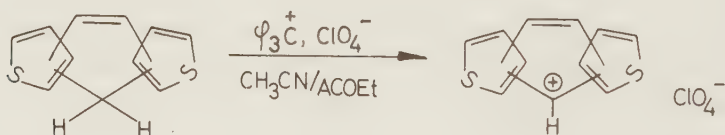
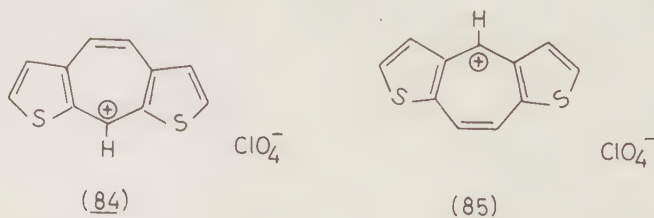
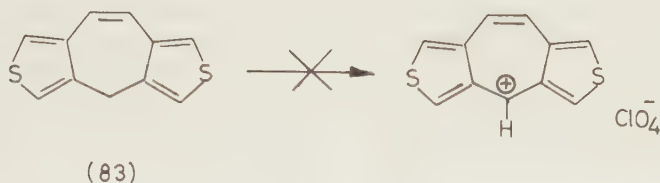


Figure 1_{IV}

The cycloheptadithiophenes (81) and (82) furnished by this method the corresponding salts: dithieno[2,1-b;4,5-b']tropylium perchlorate (84) and dithieno [1,2-b;5,4-b']tropylium perchlorate (85) in quantitative yields, simply by addition of trityl perchlorate, dissolved in acetonitrile, to a solution of the hydrocarbon in ethyl acetate.



This procedure failed when it was applied to obtain the C-annelated dithienotropylium perchlorate from the hydrocarbon (83).



A black, high melting (mp $>350^\circ$) substance, which was not characterized, was obtained.

Whatever could have been the reason for this failure, it was not investigated. Further attempts to obtain this isomer were not made at this stage. Therefore in these reports we will confine ourselves to the investigations and results of the two b-annelated dithienotropylium ions (84) and (85).

Part 2. Aromaticity of the dithienotropylium ions

A. Qualitative observations on the stability

Some chemical and physical observations as early as the cycloheptadithiophene-one stage were indicative of the high stability of the anticipated tropylium ions derived from them.

We have pointed out previously the ease with which these ketones were obtained from their saturated precursors through bromination-dehydrobromination reactions (see Part 1 of this chapter): The driving force for the spontaneous dehydrobromination undoubtedly evolves from the fact that the newly introduced double bond becomes part of a semiaromatic cycloheptatrienylium system, and in this sense it presumably takes part to some extent in charge delocalization. From this point of view, these dithienocycloheptenones can be best represented as in Fig 2_{IV}.



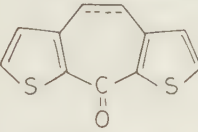
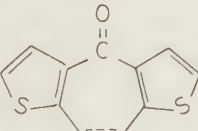
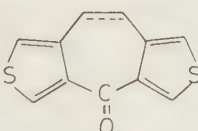
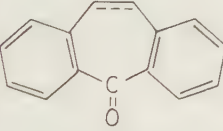
Figure 2_{IV}

Evidence for the strong polarization of the carbonyl group in these ketones comes from the ease with which they are reduced to the methylene derivatives by LiAlH_4 but not to the corresponding carbinols, as would be expected for an "ordinary" carbonyl group. And also, from the large shift to lower frequencies of the C-O-stretching bands as compared to the C-O-stretchings of the saturated precursors. These C-O-stretching bands of the unsaturated ketones, whose frequencies are among the lowest which have been observed for ketonic carbonyls (see Table 1_{IV}), suggest a high degree of single-bond character for the C-O bonds concerned, which means a highly polarized C-O bond.

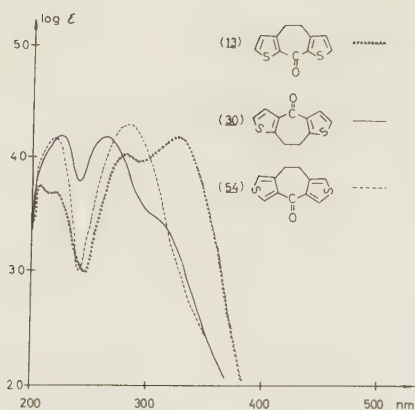
Obviously the degree of polarization is directly related to the extent to which positive charge is delocalized through the remainder of the conjugated system. In this sense, it is not difficult to see the relationship that generally exists between the C-O-stretching frequencies of cycloheptatrienone systems and the stability of the tropylium ions derived from them.

From this connection, which previously has been pointed out by Heilbronner et al. (25), for a number of benzo homologues of tropone-tropylium, a relative estimation of stabilities for the isomeric dithieno tropyliums may be derived. Thus, the order of stability is $(84) > (85) \gg (86)$.

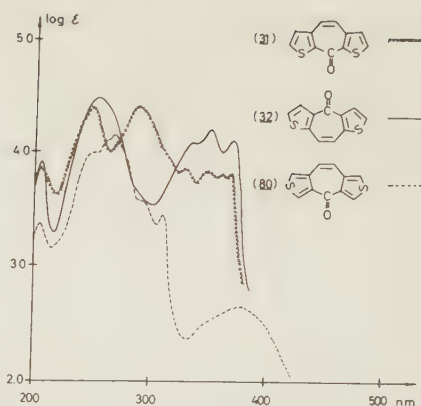
Table 1_{IV}. C-O-stretching frequencies $\bar{\nu}$

Ketones	Saturated	Unsaturated	$\Delta\bar{\nu}$
	1595 cm ⁻¹	1545 cm ⁻¹	50 cm ⁻¹
	1617 cm ⁻¹	1568 cm ⁻¹	49 cm ⁻¹
	1621 cm ⁻¹	1617 cm ⁻¹	4 cm ⁻¹
	1647 cm ⁻¹	1645 cm ⁻¹	2 cm ⁻¹

Further evidence which implies an extensive conjugation in the cycloheptadithiophene-ones, compared to the dihydro-cycloheptadithiophene-ones, is obtained from the uv spectra (Fig 3_{IV}). The fine structures between 300-400 mμ and the generally higher extinction coefficients, which are associated with the cycloheptadithiophene-ones, are consistent with a planar (75), highly conjugated ring system. Such fine structure, which is characteristic for the vibrational absorptions of polynuclear aromatic hydrocarbons with no steric inhibition of resonance, is indicative of the aromatic character of the central cycloheptenone ring.



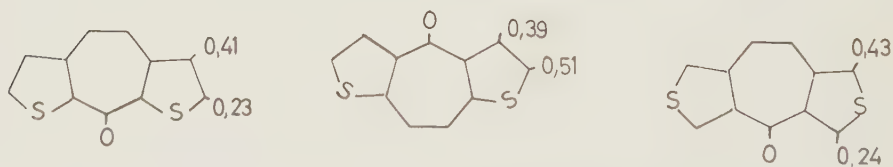
Uv spectra of dihydro-cyclo-
heptadithiophene-ones
(13), (30) and (54)
in abs. ethanol



Uv spectra of cycloheptadi-
thiophene-ones
(31), (32) and (80)
in abs. ethanol

Figure 3_{IV}

The general down-field shift of the thiophene protons in nmr (Fig 4_{IV}) which occurs on the introduction of a double bond in the dihydro-cycloheptadithiophene-ones, further supports this conclusion.

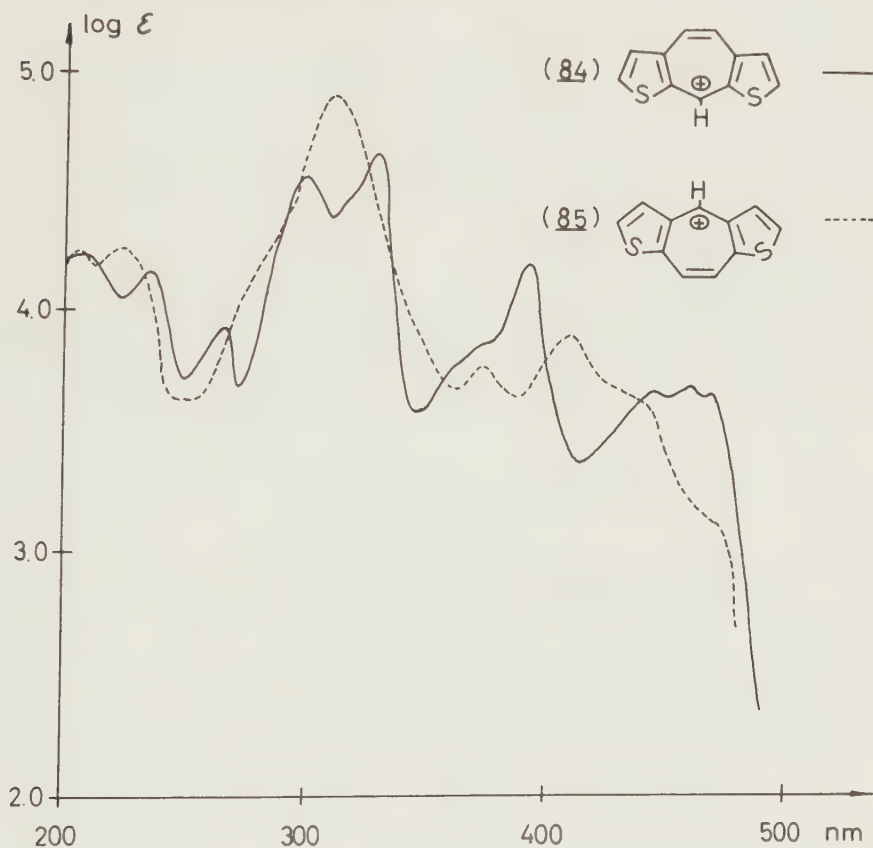


$\Delta\delta = \delta$ of cycloheptadithiophene-ones minus δ of dihydro-cyclo-
heptadithiophene-ones

Solvent: CDCl_3

Figure 4_{IV}

The uv spectra of the dithienotropylium ions (84) and (85) showed a strikingly similar pattern of absorption (Fig 5_{IV}) when compared to the uv spectra of the corresponding cycloheptadithiophene-ones (31) and (32) (Fig 3_{IV}).



Uv spectra of dithienotropylium cations (84) and (85) in conc. H_2SO_4

Figure 5_{IV}

This means that coplanarity and the aromatic properties which have been attributed to these ketones are even more profound for the derived tropylium ions.

B. Determination of the stability constants for the dithienotropylium ions

It is customary to take the acidity constant K_R^+ of a carbonium ion R^+ as a quantitative measure of its stability. In the case of a conjugated carbonium ion, the existence of a free energy relationship between the stability constant K_R^+ and the delocalization energy of R^+ can be assumed. Therefore the K_R^+ for a tropylium cation may also serve as a measure of its aromatic character.

Determination of the acidity constant, K_R^+ , is usually done by a process which essentially is a comparison of acidities of R^+ and an acid AH, whose acidity constant K_A^+ is known.

In a dilute solution the following relationships are valid:



1:

$$\therefore K = \frac{(A^+) (RH)}{(R^+) (AH)}$$

It can easily be shown that:

$$\frac{(A^+) (RH)}{(R^+) (AH)} = \frac{K_A^+}{K_R^+} = K$$

2:

$$\therefore \log \frac{(A^+)}{(R^+)} = \log \frac{(AH)}{(RH)} + \log K$$

The value of $\log K$ in equation 2 is given by the intercept of a plot of $\log \frac{(A^+)}{(R^+)}$ vs. $\log \frac{(AH)}{(RH)}$, from which the pK_R^+ can be calculated:

$$\log K = \log \frac{K_A^+}{K_R^+}$$

3:

$$\therefore pK_R^+ = \log K + pK_A^+$$

This treatment, which is valid for very dilute solutions, in which the activity coefficients $\gamma \rightarrow 1$, has a limitation which is actually the limit of the accuracy with which the equilibrium concentrations in the ratios $\frac{(A^+)}{(R^+)}$ and $\frac{(AH)}{(RH)}$ can be measured.

These concentrations are determined by the ratio $\frac{K_A^+}{K_R^+}$ (eq. 2)

and therefore in order to be able to determine accurate values for them, by using spectroscopic or potentiometric methods, the value $|pK_R^+ - pK_A^+|$ should not be too large, since otherwise concentrations on one side of the equilibrium equation might be too small to measure. A difference of 0-3 pK units in spectroscopic determinations (0-1 if by nmr) is the optimum range.

Naturally solvents with suitable acidity may serve as a reference as well.

Carbonium ions with $3 < pK_R^+ < 9$ in water solution may be determined by potentiometric titration, with dilute aqueous alkali, as may be seen from:



4:

$$K_R^+ = \frac{(H_3O^+) (ROH)}{(R^+)}$$

$$\therefore pH = pK_R^+ + \log \frac{(ROH)}{(R^+)}$$

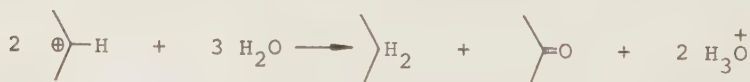
In this special case, the pK_R^+ value is given at any titration point in which the ratio $\frac{(ROH)}{(R^+)}$ and the pH of the solution are known. At the point where the amount of carbonium ion, R^+ , is equal to that of the conjugated base, namely $(R^+) = (ROH)$, the pK_R^+ is given by the value of the pH at that point. In practice this point coincides with the point in the titration curve, where half the amount of the base, for neutralization, is consumed.

The respective pK_R^+ values for the dithienotropylium perchlorates (84) and (85) were found by this method to be 6.65 ± 0.05 and 5.40 ± 0.05 at 25° in CO_2 -free aqueous solutions.

Reproducible results were obtained only when solutions under 2×10^{-4} molar were titrated. Solutions with higher concentrations of tropylium ion became turbid on standing, and the titration curves obtained from such concentrations deviated more from the classical $\int$ shape, the more concentrated the solution was. Furthermore, lower values for pK_R^+ resulted from the more concentrated solutions. Such solutions once neutralized failed to regain fully the original yellow colour of the tropylium ion upon acidification with mineral acids. Therefore there were no doubts that some irreversible reaction was taking place in the aqueous solutions, the rate of which depended on the concentration of the tropylium ion and probably on that of the conjugated pseudo-base as well.

It should be emphasized here that this behaviour was common for both dithienotropylium ions (84) and (85), though it was somewhat more marked for the former ion than for the latter.

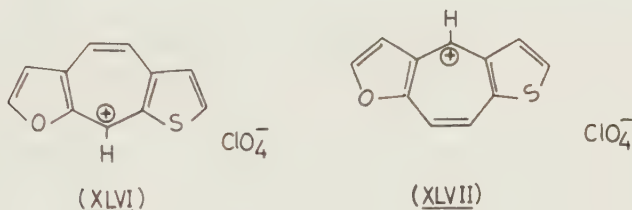
Some preliminary investigations concerning the nature of the irreversible reaction occurring in aqueous solutions of these tropylium ions suggest a sort of disproportionation, which probably involves both the carbonium ion and the pseudo-base in a bimolecular hydride transfer.



This may explain the observed higher reaction rate for higher tropylium concentrations in water as well as the lower pK_R^+ values which were obtained in such solutions.

However, further investigation is needed in order to establish the validity of this proposal.

Calculations on the dithienotropylium ions (84) and (85) as well as the analogous furothienotropylium ions (XLVI) and (XLVII) which also have been prepared in these laboratories (44), were performed both by HMO and by the ω -technique.



The following parameters for sulphur: $h_S = 1.0$, $k_{C-S} = 0.4$ and for oxygen: $h_O = 2$, $k_{C-O} = 0.6$ were used in these calculations.

In Table 2_{IV} the measured pK_R^+ values of the four tropylium ions and the calculated delocalization energies ΔE_π (π energy difference between the carbinol and the corresponding cation in β units) are recorded.

Although the linear relationship between delocalization energies (ΔE_π s) and the corresponding pK_R^+ values cannot be seen here as anticipated (76), a parallel relationship between them however is evident

Table 2_{IV}. Measured pK_R^+ values and calculated delocalization energy values ΔE_π for dithieno- and furothienotropylium ions

Cation	pK_R^+	ΔE_π	
		HMO	ω -techn
(<u>84</u>)	6.65	1.50	2.64
(<u>85</u>)	5.40	1.37	2.58
(XLVI)	6.9	1.50	2.63
(XLVII)	6.8	1.37	2.57

Part 3. Electrophilic substitution of the dithienotropylium ions

In Chapter 1 a rough estimation of reactivity towards electrophilic substitution for the different positions of dithienotropylium ions was made.

On the basis of simple resonance considerations, it was concluded that, in the two isomeric b-annelated dithienotropylium ions (84) and (85), the β -thiophenic positions are the most susceptible for electrophilic substitution (see Fig 7_I). An apriori assumption of coplanarity for these carbonium ions was essential in order that all canonical forms in Fig 7_I would be meaningful. Empirical evidence for this assumption came indirectly from the spectroscopic properties as well as the high stabilities exhibited by these ions (see Part 2 of this chapter) and directly from the X-ray analyses, which reveal a high degree of planarity for (84), so that no point of the cation's surface deviates more than 0.05 Å from the best plane (77). For (85), though still under investigation, preliminary results indicate a similar degree of planarity.

Two reactivity indices which were available directly from the HMO calculations (ω -technique), namely electron densities and superdelocalizabilities (76, pp 330), supported unequivocally reactivity predictions, which were made on the basis of simple resonance considerations.

Both indices (Fig 6_{IV}) predict higher reactivity for β -thiophenic positions toward electrophiles in (84) and (85).

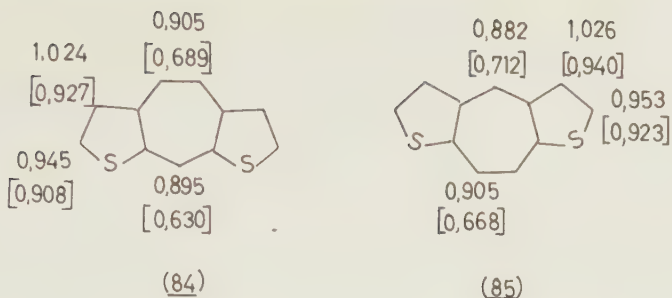


Figure 6_{IV}. Electron densities and superdelocalizabilities [Sr[⊕]] for electrophilic substitution for the dithienotropylium cations (84) and (85)

Since both (84) and (85) were easily soluble and also highly stable in concentrated mineral acids, it was natural to choose conc. D₂SO₄ both as solvent and as electrophile-source, in order to test the scope and the reliability of the foregoing reactivity predictions.

Following the substitution by nmr, it was found for both systems that:

- 1) No detectable exchange occurred in either system at room temperature (about 25°) after 24 hrs.
- 2) If the samples were kept at 68°, exchange was approximately 10 % after one hour, and was complete after 24 hrs.

The deuterating process which could be followed by nmr showed a similar pattern for both ions (84) and (85). The thiophenic doublet at higher field vanished completely, while a singlet which simultaneously grew up in the middle of the lower field doublet eventually replaced this doublet.

The growing-rate of the singlet was equal to the vanishing-rates of the doublets. This singlet was the only thiophenic signal which remained after 24 hrs at 68°. It had a relative intensity of [2H]. From all these facts, it could be concluded that, in the first place, substitution occurs preferably at one of the two thiophenic positions in both samples.

And secondly, the fact that the chemical shifts of the unsubstituted positions remain unchanged in both spectra implies

that we are actually dealing with deuterium-exchange and no other electrophilic species are involved.

The traditional shift assignments for thiophenic protons, namely the doublet at lower field to α -protons, and the doublet at the higher field to β -protons, would be consistent with deuteration at β -thiophenic positions in both samples. Nevertheless, dealing with fully-charged species, in which an extensive uneven charge delocalization is taking place, it could be argued that the usual thiophene assignments may not be taken for granted for the molecules under consideration. Therefore authentic β -deuterated dithienotropylium ions (d-84) and (d-85) were synthesized (see Schemes 2_{IV} and 4_{IV} respectively).

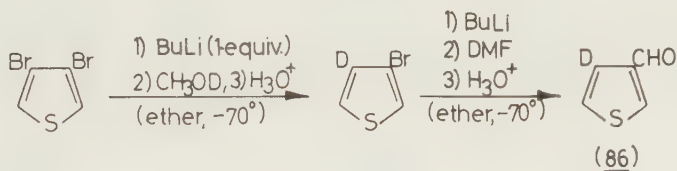
The nmr spectra of (d-84) and (d-85) which were taken in H_2SO_4 were identical with the spectra of the samples under investigation after they were partially deuterated in conc. D_2SO_4 .

Conclusions from this investigation, as far as chemical reactivity of the dithienotropylium ions (84) and (85) is concerned, are straightforward. The excellent agreement between the experiments and the theoretical predictions, as based on resonance as well as quantum mechanical calculations, is noteworthy. In the nmr spectra of the investigation sample of (84), after keeping it more than 100 hrs in D_2SO_4 and 68° , there were no noticeable changes beyond what was observed already after 24 hrs (namely fully deuterated β -thiophenic positions). In contrast, when sample of (85) was kept for 100 hrs under the same conditions, two or more new peaks near each of the three original peaks of the fully β -deuterated molecule, appeared. These new peaks, which roughly amounted to 10-15 % of the original sample, could perhaps be attributed to mono- and disulphonated products, in which probably β -deuterated positions were attacked. The fact that these apparent sulphonations were more visible for (85) than for (84) can be rationalized by the considerably higher $[\text{Sr}^\oplus]$ for the β -thiophenic position in the former (see Fig 6_{IV}). At this stage, more speculations about these latter aspects can not be made. Further preparative and perhaps also comparative-kinetic studies concerning electrophilic substitution rates for the two systems, are necessary before all the questions can be settled. These are planned as future projects.

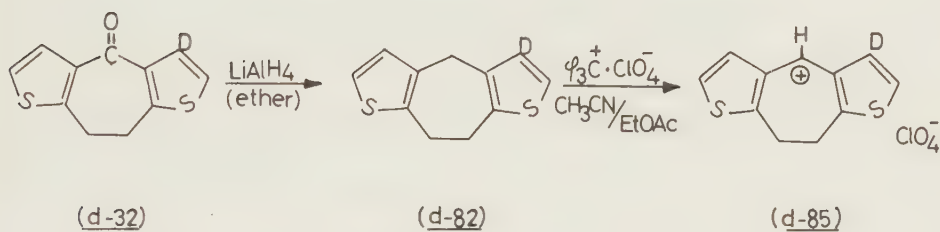
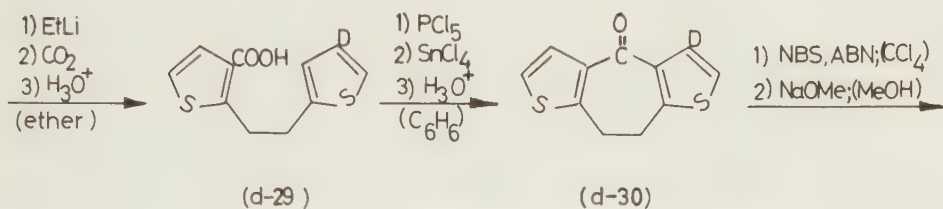
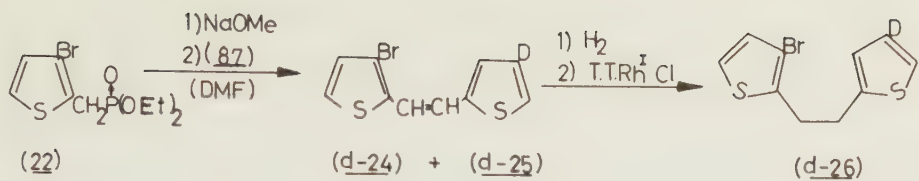
All the reactions by which the authentic β -deuterated tropylium ions (d -84) and (d -85) were prepared have been described earlier. These reactions are summarized in Schemes 2_{IV} and 4_{IV}.

The aldehydes, 4-deutero-3-thiophenealdehyde (86) and 4-deutero-2-thiophenealdehyde (87), which have been used as starting materials in syntheses of the deuterated compounds, were prepared from the corresponding dibromothiophenes by reactions which are given respectively in Schemes 1_{IV} and 3_{IV}.

Of special interest is the method in which aldehyde (87) was prepared in a one-pot reaction. This procedure, which has been applied earlier in these laboratories (43) for syntheses of certain substituted thiophenealdehydes, is shown again to be of wide utility in saving time-consuming steps in the preparation of such β -substituted thiophenealdehydes.



Scheme 1_{IV}



Scheme 4_{IV}

On 3-methylaminopropylidene derivatives of dihydro-cyclohepta-
dithiophenes

A. 3-Dimethylaminopropylidene derivatives

The synthesis of these derivatives was carried out according to the reaction sequence described briefly in Chapter I (Fig 9_I).

Description of biological properties of these compounds, which have been investigated elsewhere (78) does not belong to the frame of this work. Discussion will therefore be confined mainly to their synthetic aspects.

Generally speaking, the ketone, the derivative of which was desired, was reacted with 3-dimethylaminopropylmagnesium chloride in tetrahydrofuran solution, followed by hydrolysis in an aqueous solution of ammonium chloride.

The corresponding carbinol, obtained in this way, easily lost one molecule of water upon treatment with ethanolic hydrochloric acid.

The Grignard reagent, 3-dimethylaminopropylmagnesium chloride, was prepared in the usual manner from the corresponding chloride in dry tetrahydrofuran.

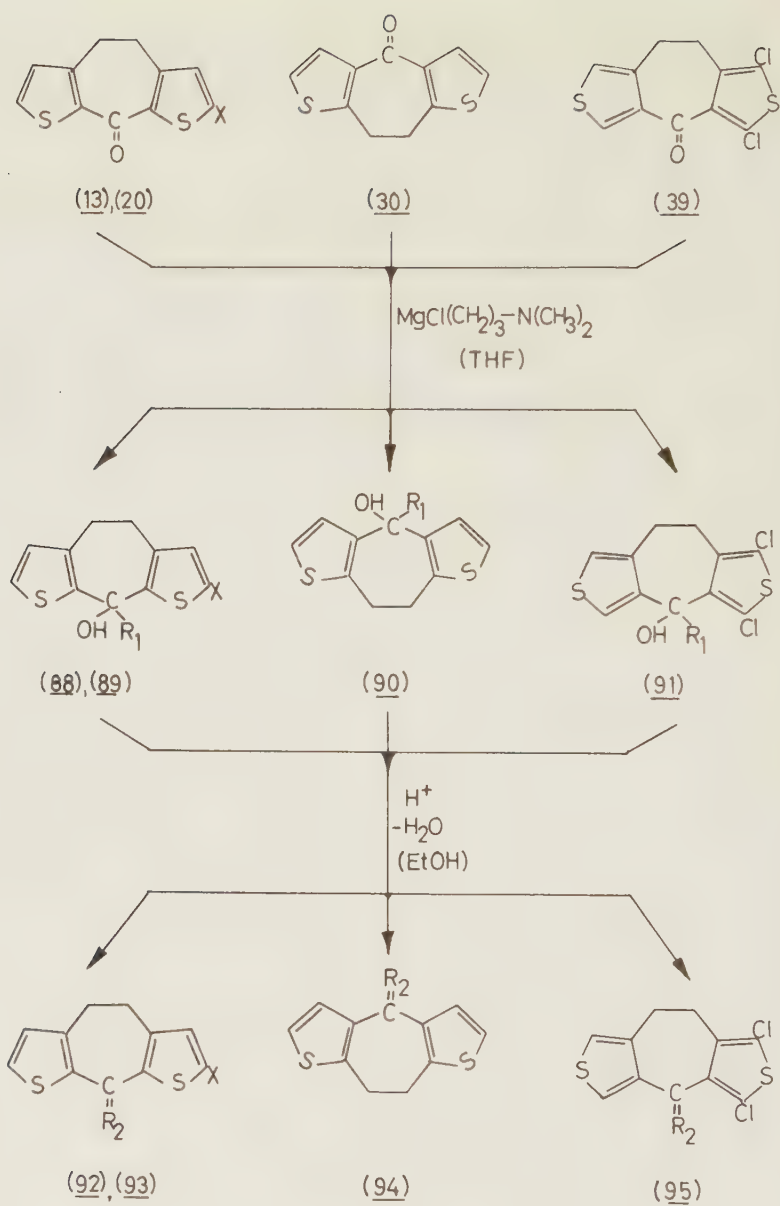
It has been reported by Bastian et al. (18) that 2-bromo-4H-benzo[4,5]cyclohepta[1,2-b]thiophene-4-one underwent halogen-metal exchange at the 2-position, when treated with 3-dimethylaminomagnesium chloride, and consequently the unsubstituted carbinol resulted upon hydrolysis.

Similar halogen-metal interconversion was not observed when ketones (20) and (39) were reacted with 3-dimethylaminopropylmagnesium chloride, even though an excess of the reagent was usually present in the reaction mixture.

The carbinols (88), (89), (90) and (91) (see Scheme 1_V) were obtained from the ketones (13), (20), (30) and (39) respectively, which upon dehydration gave the corresponding γ -dimethylaminopropylidene derivatives (92), (93), (94) and (95).

As would be expected, dehydration of (89) and (91) gave rise to cis-trans isomers, which in both cases could be seen from analyses of nmr spectra. From these analyses the isomer ratios were estimated as well, which amounted to about 2:3 for both (93) and (95).

Cis-trans structural assignment was not made.



$\text{X} = \text{H}, \text{Cl}$

$\text{R}_1 = \text{CH}_2\text{CH}_2\text{CH}_2\text{N}(\text{CH}_3)_2$

$\text{R}_2 = \text{R}_1 \text{ minus H}$

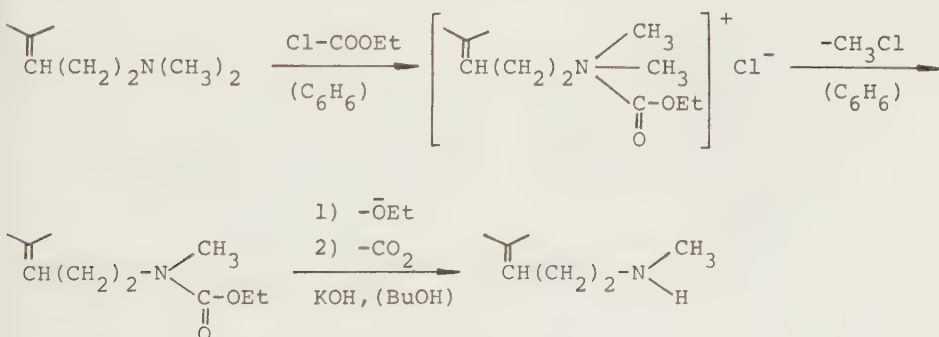
Scheme 1_V

B. 3-Monomethylaminopropylidene derivatives

An attempt was also made to prepare the monomethylamino derivatives of (92), (93), (94) and (95) which formally may be considered the dithieno analogues of Nortriptyline (VIII). The method used in order to obtain these monomethyl derivatives has been applied previously by Protiva et al. (79) and later by Bastian et al. (18) for conversion of 3-dimethylaminopropylidene derivatives to the corresponding monomethylaminopropylidene derivatives.

This so-called demethylating method was originally a modification of the procedure of Stach and Bickelhaupt (80) to eliminate a benzyl group from (3-benzylmethylaminopropylidene) derivatives.

When ethyl-chloroformate was added to a benzene solution of the dimethylamino derivative, a solid material was formed almost immediately. This solid material, which is apparently the quaternary amine product due to addition of ethyl chloroformate to the amine group, reacted slowly upon refluxing, by loss of a molecule of methylchloride (see Scheme 2_V). The ethyl



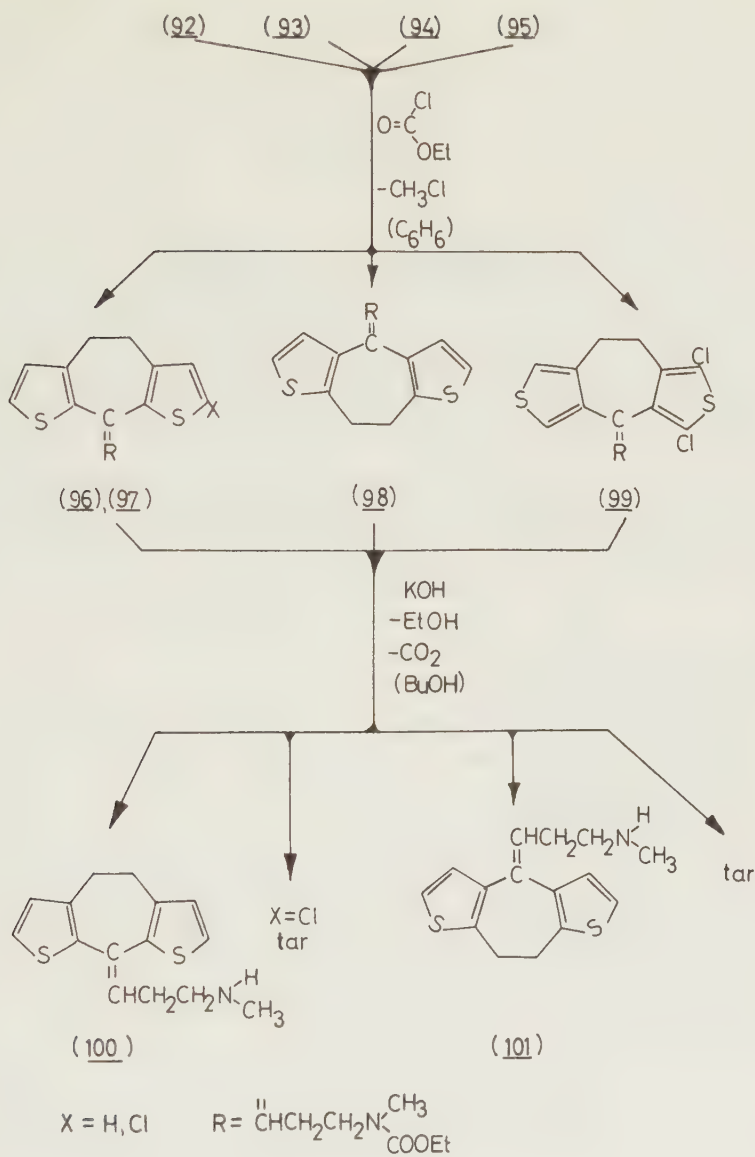
Scheme 2_V

carbamate which remained after evaporation of the benzene solution was hydrolyzed and decarboxylated in a one-pot reaction by refluxing a butanolic solution of KOH. The monomethylamino derivative was obtained usually in about 60 % yield:

Whereas by this method we were able to prepare the 3-monomethylaminopropylidene derivatives (100) and (101) (Scheme 3_V) through decarboxylative hydrolyses of carbamate precursors (96) and (98), a tar resulted when (97) and (99) were treated with KOH under the same reaction conditions.

Destruction of the molecules (97) and (99) is apparently due to the sensitivity of the α -halogenated thiophene rings in these molecules.

Since the preliminary biological tests of these compounds did not justify the pharmacological expectations, further investigation of this project was postponed.



Scheme 3_v

CHAPTER VI

Experimental

All temperature readings are uncorrected. Nmr spectra were recorded on a Varian A-60, mass spectra on an LKB 9000, ir on a Perkin-Elmer 257 Grating spectrophotometer and uv spectra on a Unicam SP 800B UV spectrophotometer. Glc analyses were performed on a Perkin-Elmer 900 Gas Chromatograph. The only column used throughout this work was: Butane-1,4-diol succinate (BDS, 10 %) on Chromosorb W. In the pK_R^+ determinations, sample-titrations were made in a titration-assembly consisting of a Radiometer Autoburette, ABU 11, in conjunction with a Radiometer pH-meter 26. Radiometer electrodes G202C and K410 were used.

List of abbreviations

ABN = Azobisisobutyronitrile

NBS = N-Bromosuccinimide

DMF = Dimethylformamide

DMSO = Dimethylsulphoxide

NCS = N-Chlorosuccinimide

T.T.Rh^ICl = Tris-(triphenylphosphine)chlororhodium^(I)

THF = Tetrahydrofuran

P.E. = Petroleum ether

BuLi = n-Butyllithium

EtLi = Ethyllithium

Section A. Preliminary attempts towards preparation of (13)

No 1. 3,3'-Thenoin condensation (XXI)

Campaigne-LeSuer's procedure (34) was slightly modified in order to obtain a better yield. To a solution of 10 g of sodium cyanide in 25 ml of water, 11.4 g (0.1 mole) of 3-thenaldehyde in 110 ml ethanol was added. This homogeneous solution was refluxed gently with effective stirring for 1 3/4 - 2 hrs and then poured slowly onto ice water, while this was stirred vigorously. After keeping it cold over night, the yellow solid was separated from the rest by suction. The crude yield was 5.6 g (49 %) (lit. (34) 33 %). Mp 114-15° (lit. (34) 116-17°).

No 2. 3-Thenyl-3'-thienyl ketone (desoxy-3,3'-thenoin) (1)

Method A (36). To a solution of 2.5 g of thenoin (0.11 mole) in 25 ml of ethanol, 8 g of SnCl_2 followed by 25 ml of conc. hydrochloric acid, was added. The reaction mixture was refluxed 1.5 hrs with stirring. It was cooled and poured onto 150-200 ml of ice water. The product was extracted with ether and the combined ethereal extracts were washed with water, sodium bicarbonate solution and water again until neutral, dried (MgSO_4) and evaporated. The residue (oily product) was recrystallized from ethanol, and furnished 1.9 g, ~85 %, of tan plate-like crystals. Mp (EtOH) 75°.

Anal. Calcd. for $\text{C}_{10}\text{H}_8\text{OS}_2$ (M.W. = 208.30): C 57.66; H 3.87; S 30.79. Found: C 57.60; H 4.00; S 30.80. Ir (KBr) 1675 cm^{-1} ($\text{C}=\text{O}$), nmr (acetone- d_6): δ 4.1 [d., 2, $J = 0.6\text{ Hz}$ ($-\text{CH}_2$)], 6.9 [d. of d., 1, $J = 1.6\text{ Hz}$, $J = 4.7\text{ Hz}$, (4-thenyl)], 7.2 [d. of d., 1, $J = 1.8\text{ Hz}$, $J = 4.7\text{ Hz}$, (5-thenyl)], 7.2 [m, 1, (2-thenyl)], 7.3 [d. of d., 1, $J = 2.8\text{ Hz}$, $J = 5.1\text{ Hz}$, (5-thienyl)], 7.5 [d. of d., 1, $J = 1.6\text{ Hz}$, $J = 5.1\text{ Hz}$, (4-thienyl)], 8.3 [d. of d., 1, $J = 1.6\text{ Hz}$, $J = 2.8\text{ Hz}$, (2-thienyl)].

Method B (37). The same procedure as in Method A was repeated, except that 8 g of Sn with a few crystals of CuSO_4 was used for reduction instead of SnCl_2 in No 2. This gave 1.8 g (80 %) of the desoxythenoin (1).

No 3. sym-Di-(3-thienyl) ethane-diol (2)

To a solution of 1.1 g of lithium aluminium hydride and 7.7 g of aluminium chloride in 50 ml of dry ether, 2.24 g (0.01 mole) of 3,3'-thenoin was added in small portions. After the spontaneous reflux had ceased, the mixture was further refluxed on a hot water bath for 1/2 hour. The excess of the reducing complex was then decomposed, carefully, by adding small pieces of ice through the condenser, to the ice-cooled reaction mixture. The ethereal layer was then decanted, and the residue was poured into aqueous H_2SO_4 20 % and extracted with 2 x 250 ml ether. The combined ether solution was washed with water until neutral, dried (MgSO_4) and evaporated. A white crystalline product started crystallizing out of the ether solution during the evaporation. Evaporation of the solvent furnished 2 g (90 %) of the corresponding diol (2), but not the dithienylethane (XXII) as expected (38): mp (ether) 138° , ir 3300 cm^{-1} (O-H), nmr (acetone- d_6): δ 4.3 [s., 2, (O-H)], 4.9 [s., 2, (-CH-O-)], 7.0 [d. of d., 2, $J = 1.5\text{ Hz}$, $J = 4.6\text{ Hz}$, (4-thiophene)], 7.1 [d. of d., 2, $J = 1.5\text{ Hz}$, $J = 3\text{ Hz}$, (2-thiophene)], 7.3 [d. of d., 2, $J = 3\text{ Hz}$, $J = 4.6\text{ Hz}$, (5-thiophene)].

Anal. Calcd. for $\text{C}_{10}\text{H}_{10}\text{O}_2\text{S}_2$ (M.W. = 226.32): C 53.07; H 4.46; S 28.33. Found: C 53.20; H 4.59; S 28.30.

No 4. sym-Di-(3-thienyl) ethane (XXII)

Desoxythenoin (1) was reduced (2.1 g, 0.01 mole) by a mixture of LiAlH_4 - AlCl_3 and worked up according to procedure No 3), giving 1.9 g (98 %) of sym-di-3-thienylethane (XXII), which upon recrystallization from MeOH-water gave mp 66° (lit. (34) $64\text{--}65^\circ$).

No 5. sym-Di-(2-bromo-3-thienyl) ethane (3)

6.68 g (34.4 mmole) of (XXII) dissolved in 40 ml of a 1:1 mixture of chloroform and acetic acid, and 12.8 g (72 mmole) of NBS was added in one portion. The reaction mixture was cooled with water and stirred for 15 min. The mixture was poured onto 100 ml of water, the layers were separated and the aqueous phase was extracted twice with chloroform. The combined organic phases were washed with water (3 x 30 ml), dried over MgSO_4 and evaporated, to yield 12.0 g of solid. Treatment of this solid with pentane and cooling gave 11.2 g (93 %) of colourless solid, mp 50.5° , nmr (CDCl_3): δ 2.8 [s., 4, ($-\text{CH}_2-\text{CH}_2-$)], 6.7 [d., 2, $J = 5.5$ Hz, (4-thiophene)], 7.1 [d., 2, $J = 5.5$ Hz, (5-thiophene)].

Anal. Calcd. for $\text{C}_{10}\text{H}_8\text{Br}_2\text{S}_2$ (M.W. = 352.14): C 34.11; H 2.29; Br 45.39; S 18.21. Found: C 34.3; H 2.27; Br 45.40; S 18.10.

Section B. Starting materials for the olefin syntheses

No 1. (2-Bromo-5-chloro)-3-methylthiophene (14)

To 88.5 g (0.05 mole) of 2-bromo-3-methylthiophene dissolved in 300 ml of acetic acid, 66.75 g (0.5 mole) of NCS was added in one portion. The reaction mixture was stirred at 40° for about 2 hrs and then refluxed 1 hr. It was poured into 1500 ml water, and extracted with ether (3 x 500 ml). The combined ether layers were washed with 1 N NaOH solution (4 x 300 ml), then water until neutral, dried over Na₂SO₄ and distilled. The main fraction, which boiled at 76-81°/10 mm, yielded 84.6 g (80 %), a smaller fraction (10.6 g) which boiled at 81-86°/10 mm appeared to be practically identical with the main fraction. The over all yield was 95.5 g (90 %), b.p. 79° (10 mm), $n_D^{20} = 1.5730$, nmr (CDCl₃): δ 6.5 [s., 1, (4-thiophene)], 2.1 [s., 3, (-CH₃)].

No 2. 4-Bromo-3-methylthiophene (40)

To a solution of 96.8 g (0.4 mole) of 3,4-dibromothiophene in 100 ml of ether, 690 ml of 0.74 N BuLi was added dropwise at -70° during 20 min. After stirring 30-40 min more, 63.5 g of freshly distilled dimethylsulphate in an equal volume of ether was added during 5-10 min. The reaction mixture was stirred at -70°C for 3 more hrs, and then the cooling bath was removed. Stirring was continued until the mixture reached room temperature. It was then poured into a well-stirred 0.1 N aqueous solution (800 ml) of ammonium hydroxide. After stirring for about 0.5 hr, the organic layer was separated and the aqueous layer was extracted with 2 x 250 ml of ether. The combined ethereal solutions were washed with water (2 x 300 ml), 0.1 N HCl (2 x 150 ml) and water until neutral, dried (CaCl₂), concentrated and distilled, giving 54.6 g (77 %) of the 3-bromo-4-methylthiophene, b.p. 60-63° (10 mm), $n_D^{20} 1.5797$ lit. (50) b.p. 181-184° (770 mm), $n_D^{20} 1.5795$, nmr (CDCl₃): δ 2.2 [d., 3, J = 1 Hz, (-CH₃)], 6.8 [d. of q., 1, J = 1 Hz, J = 3.5 Hz, (2-thiophene)], 7.1 [d., 1, J = 3.5 Hz, (5-thiophene)].

No 3. 2-Chloro-3-bromothiophene (55)

163 g of 3-bromothiophene (1 mole) and an equivalent amount (133.5 g) of N-chlorosuccinimide in 500 ml of a 1:1 mixture of acetic acid/carbon tetrachloride was heated until spontaneous reflux started. It was stirred efficiently as long as spontaneous refluxing continued, and when it ceased, the reaction mixture was heated to maintain reflux for a further 30 min. The reaction mixture was cooled and poured into 1.5 litres of ice-water (stirring). The organic layer was separated, washed with water, 0.5 N NaOH solution and water until neutral, dried (CaCl_2), concentrated and distilled. The main fraction (127.5 g) was collected at 68-72° (9 mm) and a second fraction (21 g, 90 % pure) was collected at 72-75° (9 mm). The overall yield was 148.5 g (75 %), n_D^{25} 1.5957, b.p. 70° (9 mm), nmr (CDCl_3): δ 6.8 [d., 1, J = 6 Hz, (4-thiophene)], 7.2 [d., 1, J = 6 Hz, (5-thiophene)].

No 4. 2-Chloro-3-thienaldehyde (46)

2-Chloro-3-thienyllithium, which was prepared from 79 g (0.4 mole) of 2-chloro-3-bromothiophene (55) in ether solution (200 ml) and 660 ml of 0.72 N EtLi in the usual manner (45), was treated with 40 g of water-free DMF in ether (100 ml) by rapid addition (at -70°). After 15 min of stirring the cooling bath was removed, and stirring was continued until the reaction mixture reached room temperature. It was then poured into 800 ml of a 0.5 N ice-water solution of hydrochloric acid. It was worked up as usual and distilled. The fraction boiling at 57-62° (0.1 mm) was collected, giving 54 g (92 %) of pure aldehyde. Most of the product, however, distilled at b.p. 60-62° (0.1 mm), n_D^{25} 1.5940 [lit. (48) n_D^{20} 1.5908, b.p. 100-102° (1-2 mm)], ir (film) 1670, 1690 ($-\text{CHO}$). Nmr (CDCl_3): δ 7.1 [d. of d., 1, J = 6 Hz, J = 0.8 Hz, (4-thiophene)], 7.2 [d., 1, J = 6 Hz, (5-thiophene)], 10.0 [d., 1, J = 0.8 Hz ($-\text{CHO}$)].

No 5. 4-Deutero-3-thenaldehyde (86)

This compound was obtained from 4-deutero-3-bromothiophene (50), in a modification of Gronowitz's procedure (45) for 3-thenaldehyde.

To the 4-deutero-3-thenyllithium derivative, which was formed in the usual manner by halogen-metal interconversion between 49.2 g (0.3 mole) of 4-deutero-3-bromothiophene in ether solution (200 ml), and 475 ml of 0.7 N BuLi in ether, 36 g of water-free DMF in ether (100 ml) was added during 5 min with effective stirring. The cooling bath was removed after 30 min, stirring was continued until the reaction mixture reached room temperature, and was then decomposed by pouring into a 20 % ice-water solution of ammonium chloride. After the usual work-up, the concentrated ethereal layer was distilled, giving 24 g (70 %) of 4-deutero-3-thenaldehyde, b.p. 40-45° (1 mm) [lit. (45) 86-87° (20 mm)], nmr (CDCl₃): δ 7.3 [d. of q. of m., 1, J = 3 Hz, J = 0.8 Hz, J = 0.7 (5-thiophene)], 8.1 [d., 1, J = 3 Hz, (2-thiophene)], 9.8 [d., 1, J = 0.8 Hz, (-CHO)].

No 6. 4-Deutero-2-thenaldehyde (87)

A solution of 42.2 g (0.17 mole) 2,4-dibromothiophene in 100 ml of ether (abs.) was cooled to -70° under a nitrogen atmosphere, and to it was added 110 ml of 1.6 N BuLi (in hexane) during 20 min. It was stirred an additional 15 min at -70°, and then 13 g of abs. DMF dissolved in 100 ml of ether was added to it quickly. The cooling bath was removed at this stage and the mixture was stirred for 30 min. After this period the reaction mixture was recooled to -70°, and a second portion of 172 ml of the 1.6 N BuLi was added dropwise during 10-15 min. Stirring was continued for another 75 min, and 8.0 g of CH₃OD in 50 ml of ether was added. The cooling bath was removed, and the complex was decomposed when it reached room temperature, by pouring it into a well-stirred 20 % ice-water solution of ammonium chloride. The work-up was as usual. Distillation of the crude product gave a fraction (10 g), which boiled at

90-110° (15 mm). Glc analysis showed that 20 % starting material was present. Redistillation at 95-102° (15 mm) gave ~8 g (41 %) 4-deutero-2-thienaldehyde which was pure enough (>95 %) for further use. Nmr (CDCl₃): δ 7.8 [s., (broad), 2, (3- and 5-thiophene)], 9.9 [d., 1, J = 1 Hz (-CHO)].

No 7. 3-Thenylbromide (XXIV)

Compound 3-methylthiophene was side-chain brominated according to Campaigne and LeSuer (34), ABN was used as radical initiator.

No 8. 2-Bromo-3-thenylbromide (XXIII)

The compound was prepared by side-chain bromination of 2-bromo-3-methylthiophene (81) using the Gronowitz (45) procedure. B.p. 120-125°C (11 mm). [Lit. (45) b.p. 88-90°C (4 mm)]. ABN was used as radical initiator.

No 9. 2-Bromo-5-chloro -3-thenylbromide (15)

Gronowitz's method (45) for 2-bromo-3-thenylbromide (XXIII), was slightly modified. Thus to a solution of 95.2 g (0.45 mole) of 2-bromo-5-chloro -3-methylthiophene (14) in 400 ml of carbon tetrachloride, a mixture of 0.8 g ABN and 80 g NBS was added, and the reaction mixture refluxed for 5 min. A second portion of 0.8 g of ABN was added through the condensor. After a few minutes the reaction became spontaneous and heating should therefore be adjusted in order to maintain a gentle reflux (stop the heating, if necessary). After about 3 hrs' reflux with stirring the reaction mixture was cooled to room temperature and the floating succinimide was filtered, washed with carbon tetrachloride (2 x 50 ml) and the combined organic solutions were washed with 0.5 N solution of sodium bicarbonate (3 x 200 ml) to remove any dissolved succinimide, and then with water, until neutral, dried (CaCl₂), concentrated and distilled. The fraction boiling at 128-135°C (10 mm) was collected. Most of the product however distilled at 132°C (10 mm), giving 112.7 g (86.2 %), which was practically pure for further use. Nmr (CDCl₃): δ 4.2 [s., 2, (-CH₂-)], 6.8 [s., 1, (4-thiophene)].

No 10. 2-Thenyl chloride (XXVIII)

This compound was prepared by chloromethylation of thio-
phene by the method of Wiberg and McShane (82).

No 11. 3-Bromo-2-thenylchloride (XXVII)

This compound was obtained from chloromethylation of
3-bromothiophene according to the method reported by Wynberg
and Kraak (83).

No 12. 2,5-Dichloro-3-thenylchloride (XXXII)

2,5-Dichlorothiophene (84) was chloromethylated by the
method of Gronowitz (45).

No 13. 4-Bromo-3-thenylbromide (41)

Side-chain bromination of 4-bromo-3-methylthiophene (40)
was carried out in the same manner as for the preparation of
2-bromo-5-chloro -3-thenylbromide (15) in No 9. In distilling
the worked-up reaction product, 30.5 % of the starting material
(40) boiling at 34°C (0.5 mm) was recovered. The desired pro-
duct (41) came as the second fraction, b.p. 80-90° (0.2 mm)
or 110-136° (10 mm), and gave ~60 % reasonably pure product.
A higher boiling fraction which was also obtained was not
investigated. Nmr (CDCl₃): δ 4.4 [d., 2, J = 0.5 Hz, (-CH₂-)],
7.2 [d., 1, J = 3.4 Hz, (2-thiophene)], 7.3 [d. of d., 1,
J = 3.4 Hz, J = 0.5 Hz, (-CH₂-)].

No 14. 2-Chloro-3-thenylbromide (XXXIII)

This compound was prepared by side-chain bromination of
2-chloro-3-methylthiophene (84), according to Campaigne and
LeSuer (48) replacing dibenzoylperoxide by ABN as radical
initiator.

No 15. A general procedure for the preparation of thenyl-
triphenylphosphonium salts (4), (6), (21), (23),
 (42) and (44)

Equivalent amounts of the corresponding thenylhalide (chloride or bromide) and triphenylphosphine, which were dissolved separately in anhydrous benzene, were mixed. The homogeneous solution (0.66 molar) obtained in this way was refluxed for 20-48 hrs (for the chlorides) under N_2 , or stirred (N_2) at room temperature (see Table 1_{VI}). The white phosphonium salt was filtered, washed once with benzene and several times with ether. A second crop was usually obtained by concentrating the mother liquor to a quarter of its original volume, refluxing 1-2 hrs and cooling overnight in the refrigerator. The nearly pure phosphonium salt was dried under reduced pressure (P_2O_5) and was used without further purification in Wittig olefin syntheses. (See also Table 1_{VI}).

Table 1_{VI}. Reaction conditions and yields in preparation of the phosphonium salts, and the mp's of the products

Phosphonium salt	Conditions		Yield %	Recrystallized from	Mp
	refluxed	stirred at room temp.			
(<u>4</u>)	-	48 hrs	92	EtOH	240°
(<u>6</u>)	-	15 hrs	91	EtOH	319°
(<u>21</u>)	48 hrs	-	88	EtOH-H ₂ O	237°
(<u>23</u>)	20 hrs	-	90	EtOH	>340°
(<u>42</u>)	12 hrs	-	91	EtOH	229°
(<u>44</u>)	12 hrs	-	89	EtOH-H ₂ O	269°

No 16. General procedure for the preparation of diethyl-
thenylphosphonates

The thenylhalide, mixed with an excess (1.3 equiv.) of triethyl phosphite, was heated under nitrogen on an oil-bath at 110-120° for one hour. The bath-temperature was then raised to 150-160°C and heating continued another 2 hrs. The products were distilled at reduced pressure. High yields of phosphonates were usually obtained. (See Table 2_{VI}).

Table 2_{VI}. Phosphonates prepared according to No 16

Phosphonate	B.p. (mm Hg)	Lit. b.p. (mm Hg)	Yield %	Refraction index
(<u>5</u>)	130-134° (0.01)	-	92	$n_D^{20} = 1.5297$
(XXV)	128-132° (1.0)	99-100° (19) (0.1)	90	$n_D^{24} = 1.4980$ (19)
(<u>16</u>)	128-134° (1.0)	-	91	-
(<u>22</u>)	116-118° (5x10 ⁻³)	-	92	-
(XXIX)	119-124° (0.5)	180-184° (31.0)	95	$n_D^{20} = 1.5037$ (85)
(<u>34</u>)	120° (0.1)	-	96	$n_D^{20} = 1.5202$
(<u>43</u>)	115-122° (5x10 ⁻³)	-	87	$n_D^{25} = 1.5280$
(<u>45</u>)	109-110° (4x10 ⁻³)	-	86	$n_D^{25} = 1.5105$

Section C. The Wittig and related syntheses

No 1. General procedure for the Wittig olefin syntheses of 1,2-dithienyl ethylenes

To a well-stirred suspension of a phosphonium salt in anhydrous DMF (100 ml solvent per 0.1 mole of phosphonium salt) an excess (1.5 equiv.) of sodium methoxide suspended in anhydrous DMF (30 ml solvent per 0.1 mole) was added at 0-5° under a nitrogen atmosphere. The phosphorane intermediate (from tan to intensive orange in colour), which was formed almost instantaneously, was stirred an additional 30 min and then an equivalent amount of aldehyde dissolved in anhydrous DMF was added dropwise at such a rate that the reaction temperature did not exceed 30°C. A few minutes after all the aldehyde was added, the cooling bath was removed, and the reaction mixture was stirred another 2 hrs at room temperature. It was then poured onto ice-water and acidified (aq. HCl, pH 3-4), extracted with ether, washed, dried (MgSO₄), and concentrated to ca. 100 ml/0.1 mole. By storing this cold overnight, most of the triphenylphosphinoxide was precipitated. After filtration, the filtrate was concentrated, and the oily residue was freed from the remaining triphenyl phosphineoxide by elution with benzene on a column packed with silica gel (ca. 5-6 g per 1 g oil) (52). The benzene solution was washed with 1 N bisulphite solution and water. It was dried (CaCl₂)* and a small portion was taken to determine the cis-trans ratio by glc** (on BDS 10 %, col. temp. 200-215°). Pure trans isomer could usually be obtained by fractional precipitation in hexane of the oily residue after evaporation. The cis isomers were obtained in crystalline form, from the hexane solution only in the case of the dibromo olefins(56), (XLI) and (XLIV), from which the trans isomer was precipitated as the first fraction. In the case of monobromo olefins, the cis

* Residue after evaporation of this solution was taken as the crude yield of the reaction as given in Table 1_{III}.

** The peak with lower retention time was always assigned to the cis isomer.

isomer did not crystallize from the hexane solution, and even fractional distillation of the isomer mixture did not give a better separation than about 85 % cis mixed with about 15 % trans. Further attempts to obtain pure cis-monobromo olefins were not made. (However, cis forms of the carbonated derivatives could be isolated). A list of the Wittig reactions which have been carried out by this general method with cis-trans isomer ratios and yields is given in Table 1_{III}.

For physical and spectral characteristics of the dithieno ethylenes obtained by this method see Table 3_{VI}.

No 2. General procedure for the Wadsworth-Horner modification to the Wittig olefin syntheses

A mixture of equivalent amounts of aldehyde and phosphonate dissolved in anhydrous DMF (100 ml/0.1 mole) was added dropwise to a cold (0-5°) suspension of sodium methoxide (1.5 equiv.) in DMF.

The reaction mixture was stirred an additional 10-15 min and the cooling bath was removed. Stirring was continued at room temperature for 1.5 hrs and then poured onto cold water. The organic layer was extracted with ether. The combined ethereal extracts were washed with a 1 N aqueous solution of bisulphite, water, and dried (CaCl₂).* The cis-trans isomer distribution of the reaction was determined by glc** (BDS 10 %, 200-215°) at this stage. The residue from the concentration of the solution often consisted of large amounts of trans isomer. It was therefore easily solidified by addition of small amounts of hexane, or could also be used crude as obtained in subsequent reactions.

In Table 2_{III}, a list of all the olefin syntheses which were carried out by this procedure, the crude yields of olefin, and cis/trans isomer distributions are given. See also Table 3_{VI} for characteristics of the olefinic products.

* Residue after evaporation of this solution was taken as the crude yield of the reaction as given in Table 2_{III}.

** The peak with lower retention time was always assigned to the cis isomer.

Table 3_{VI}. The 1,2-dithienyl-ethylenes which were synthesized according to the olefination procedures No 1 and No 2 (Section C) and their physical characteristics (see also Tables 1_{III} and 2_{III} for isomer distribution and yields)

Olefin	Mp (solvent)	B.p. (mm Hg)	Analyses and nmr (CDCl ₃)
(7)**	-	130-145° (0.4)	This isomer was not obtained in pure form
(8)**	62° (Hexane)	-	Calcd. for C ₁₀ H ₇ BrS ₂ (M.W. = 271.20): C 44.28; H 2.60; Br 29.47; S 23.65. Found: C 44.40; H 2.65; Br 29.64; S 23.40. δ 6.9 [s., 2, (-CH=CH-)], 7.1-7.3 [m., 5, (thioph.)].
trans- (17)	73.5° (P.E., 60-75°)	-	Calcd. for C ₁₀ H ₆ ClBrS ₂ (M.W. = 305.65): C 39.30; H 1.98; Hal(Cl) 23.2; S 20.98. Found: C 38.80; H 1.84; Hal(Cl) 23.80; S 21.20. δ 6.8 [s., 2, (-CH=CH-)], 6.9 [s., 1, (thioph.)], 7.2-7.3 [m., 3, (thioph.)].
(24)**	-	131-136° (0.06)	This isomer was not obtained in pure form
(25)**	53° (Hexane)	137-144° (0.06)	Calcd. for C ₁₀ H ₇ BrS ₂ (M.W. = 271.20): C 44.28; H 2.60; Br 29.47; S 23.65. Found: C 44.50; H 2.58; Br 29.50; S 23.50. Nmr unresolved.

Table 3_{VI} continued

Olefin	Mp (solvent)	B.p. (mm Hg)	Analyses and nmr (CDCl ₃)
trans- (35)	94° (Hexane)	-	Calcd. for C ₁₀ H ₅ Cl ₂ BrS ₂ (M.W. = 340.09): C 35.32; H 1.48; Hal(Cl) 31.27; S 18.85. Found: C 35.60; H 1.53; Hal(Cl) 31.20; S 18.93. δ 6.9 [m., 2, (-CH=CH-)], 7.1 [s., 1, (thioph.)], 7.3 [d., 1, J=3.4 Hz, (thioph.)], 7.4 [d., 1, J=3.4 Hz, (thioph.)].
(47)	-	130-133° (5x10 ⁻³)	Analytical sample was not prepared. δ 6.5 [s., 2, (-CH=CH-)], 6.6 [d., 1, J=6 Hz, (thioph.)], 6.9 [d., 1, J=6 Hz, (thioph.)], 7.0 [d., 1, J=3.2 Hz, (thioph.)], 7.2 [d., 1, J=3.2 Hz, (thioph.)].
(48)	121° (Hexane)	-	Calcd. for C ₁₀ H ₆ ClBrS ₂ (M.W. = 305.65): C 39.30; H 1.98; Hal(Cl) 23.20; S 20.98. Found: C 40.00; H 2.25; Hal(Cl) 23.40; S 20.90. δ 7.1 [s., 2, (-CH=CH-)], 7.1 [d., 1, J=6.5 Hz, (thioph.)], 7.3 [d., 1, J=6.5 Hz, (thioph.)], 7.3 [d., 1, J=3.5 Hz, (thio- ph.)], 7.5 [d., 1, J=3.5 Hz, (thioph.)].
cis- (56)	61° (Hexane)	130-160° (0.2)	Calcd. for C ₁₀ H ₆ Br ₂ S ₂ (M.W. = 350.09): C 34.31; H 1.72; Br 45.65; S 18.31. Found: C 35.10; H 1.80; Br 45.90; S 18.10. δ 6.7 [s., 2, (-CH=CH-)], 7.0 [d., 2, J=5.3 Hz, (thioph.)], 7.3 [d., 2, J=5.3 Hz, (thioph.)].

Table 3_{VI} continued

Olefin	Mp (solvent)	B.p. (mm Hg)	Analyses and nmr (CDCl ₃)
trans- (<u>56</u>)	154 ^o (Acetone)	-	Calcd. as for cis-(<u>56</u>). Found: C 34.10; H 1.88; Br 46.60; S 18.20. δ^* 6.9 [d., 2, J=5.2 Hz, (thioph.)], 7.1 [t., 2, J=0.5 Hz, (-CH=CH-)], 7.2 [d. of t., 2, J=5.2 Hz, J=0.5 Hz, J=0.5 Hz, (thioph.)].

* Nmr recorded in CS₂.

** The deuterated derivative was also made, but not characterized at this stage.

No 3. 1-(3-Carboxy-2-thienyl)-2-(2'-thienyl)ethylene (28)

A mixture of 11.6 g (0.05 mole) of diethyl-2-thienylphosphonate and 7.8 g (0.05 mole) of 2-formyl-3-thenoic acid in DMF solution was added dropwise to a cold (10-15°C) suspension of 6.8 g (2.5 equiv.) of sodium methoxide in 50 ml of abs. DMF at such a rate that the reaction temperature (exothermic) did not exceed 30°C. After all of the mixture was added, the cooling bath was removed and the reaction mixture was stirred an additional 75 min at room temperature.

It was poured with stirring onto 600 ml of cold water. The insoluble oily organic materials which floated on the water surface were extracted away by ether and discarded. The carboxylic acid was precipitated from the clear aqueous phase by acidifying with 0.5 N aq. HCl, in the usual manner.

After precipitation was complete (between 1-2 hrs at room temperature) the acid was filtered, and dried. The crude yield of the carboxylic acid, predominantly trans isomer (28), was 10.7 g (90 %). For physical and spectral characteristics see Tables 4_{VI} and 5_{VI} (Section D).

No 4. 1-(4-Carboxy-3-thienyl)-2-(2',5'-dichloro-3'-thienyl)-ethylene (36)

To a cold (10-15°C) suspension of 4.0 g (0.075 mole) of sodium methoxide in 30 ml of abs. DMF, a mixture of 9.1 g (0.03 mole) of diethyl-(3,5-dichloro-3'-thienyl)phosphonate and 4.7 g (0.03 mole) of 3-formyl-4-thenoic acid in abs. DMF, was added dropwise. The reaction temperature during this addition was kept under 30°C. When all of the mixture had been added and the exothermic reaction had ceased, the cooling bath was removed and the mixture was stirred at room temperature for 2 hrs.

The contents were poured onto water (600-700 ml) with efficient stirring. A turbid solution was obtained due to the low-solubility of the lithium salt of the carboxylic acid. To avoid coagulation of the acid with the insoluble particles, acidification was performed by careful addition of 0.1 N aq. HCl in small portions (at 4-5 min intervals, near the precipi-

tation point) with constant and efficient stirring. After all of the carboxylic acid was precipitated, a 50 ml portion of concentrated HCl was also added and stirring continued for an additional few hours. The solid was filtered, washed with water, and dried to give 7.0 g (85 %) of almost pure carboxylic acid (36), which behaved as a mixture of isomers (no defined melting points). Recrystallization from chloroform gave however sharp-melting (216°) crystals, which are most likely the trans isomer. Further investigation of the isomer distribution was not made. For physical and spectral constants see Tables 4_{VI} and 5_{IV} in Section D.

No 5. General method for alkylation of triphenyl-thenylidene phosphoranes

To the thenylidene phosphorane which was prepared in situ in a manner slightly different from the procedure given in No 1 (Section C) (1.1 equiv. base instead of 1.5), a solution of thenyl halide in abs. DMF was added dropwise.

The phosphorane colour disappeared slowly. After all of the thenyl chloride had been added (10-15 min), the reaction mixture was stirred one hour at room temperature and heated to $70-80^{\circ}$ for another 0.5 hr. It was again cooled (about 5°), and a second portion of 1.5 equiv. of sodium methoxide suspended in a small amount of abs. DMF, was added (still under nitrogen) through the condenser. A new phosphorane was formed (red in colour). The new phosphorane was stirred another 0.5 hr at 5° , and then decomposed by water which was added through the condenser, stirred an additional 20 min, and then the contents were poured onto water. The work-up was as described earlier in No 1. The final oily product, freed from triphenylphosphine oxide, gave upon further treatment the corresponding crystalline 1,2-dithienylethane.

No 6. sym-Di-(2-bromo-3-thienyl)ethane (3)

This compound was obtained from 51.8 g (0.1 mole) of 2-bromo-3-thienyltriphenylphosphonium bromide (4), 6 g of sodium methoxide, 25.6 g (0.1 mole) of 2-bromo-3-thienylbromide, and finally a second portion of 8.1 g of the base. Following the general procedure above (No 5) the reaction gave 14.8 g (42 %) of oily product which after recrystallization from pentane showed the same physical properties as a sample described above (see Section A).

No 7. sym-Di-(4-bromo-3-thienyl)ethane (71)

According to the general procedure in No 5, (71) was prepared from 93.2 g (0.18 mole) of 4-bromo-3-thienyl-triphenylphosphonium bromide, 10.8 g (1.1 equiv.) of sodium methoxide, 46.0 g (0.18 mole) of 4-bromo-3-thienylbromide, and finally a second portion of 14.6 g (1.5 equiv.) of sodium methoxide. After treatment of the final product in methanol, it gave 25 g (40 %) of solid material with mp (MeOH) 85°. Nmr (CDCl₃): δ 2.9 [s., 4, (-CH₂-)], 6.9 [d., 2, J = 3.2 Hz, (thiophene)], 7.2 [d., 2, J = 3.2 Hz, (thiophene)].
Anal. Calcd. for C₁₀H₈Br₂S₂ (M.W. = 352.12): C 34.11; H 2.29; Br 45.39; S 18.21. Found: C 34.20; H 2.32; Br 45.00; S 18.30.

Section D. Carbonations and hydrogenations

No 1. General procedure for the carbonation of 1-(bromo-thienyl)-2-(thienyl) ethylenes and 1-(bromo-thienyl)-2-(thienyl)-ethanes

An anhydrous ethereal solution (ca. 1 molar) of the bromo derivative was cooled to -70° under a nitrogen atmosphere. To this solution 10-15 % excess of ~ 1 N ethereal EtLi was added at a rapid dropwise rate. After all of the ethyllithium had been added, the reaction mixture was stirred an additional 10-15 min at -70° , and then poured quickly onto crushed solid carbon dioxide covered with anhydrous ether. The mixture was allowed to warm up to $2-3^{\circ}$, water and ether were added, and it was shaken in a separatory funnel until all the solids were dissolved.

The aqueous layer was separated and the ethereal layer was extracted 2-3 times with small portions (1/10 of the total volume) of aq. 1 N alkali solution. The combined aqueous phases were acidified with cold 5 N aq. HCl, and precipitation was complete after standing 2-3 hours at room temperature. The white precipitate was filtered, washed several times with distilled water, and dried thoroughly under vacuum. The yields varied from 90-95 %.

The carboxylic acids obtained in this way could usually be used in a subsequent reaction without additional purification.

A list of the acids prepared by this procedure is given in Table 4_{VI}. Physical and spectral data of the acids are given in Tables 4_{VI} and 5_{VI} respectively.

Separation of the cis from the trans in carboxylic acids, which were obtained from carbonation of the cis-enriched bromo precursors (see Section C, No 1), was carried out by fractional extraction. The isomer mixture was extracted in a Soxhlet with

hexane for 1 hr. The resulting solution, which contained mainly the cis isomer (the trans isomers were as a rule insoluble in hexane), was filtered and concentrated. The solid residue was extracted with hexane two-three subsequent times at room temperature and evaporated. By this procedure usually greater than 80 % of the cis isomer in the mixture could be isolated in essentially pure form and characterized. See Table 4_{VI} for the bromo compounds which were carbonated, the carboxylic acids obtained, and their physical characteristics. For the spectral data of the carboxylic acids, see Table 5_{VI}.

Table 4_{VI}. Physical characteristics of the carboxylic acid derivatives obtained by carbonation of their bromo precursors according to general procedure No 1, Section D

Unsaturated bromo compd. (mixture of)	Carbonated products obtained	Molecular formula (M.W.)	Mp (solvent)	Analyses %			
				C	H	S	Cl
(7), (8)	(10)	C ₁₁ H ₈ O ₂ S ₂ (236.31)	149-150 (Hexane-Ether)	Calcd.: 55.91 Found: 55.70	3.41 3.52	27.13 26.90	
	(11)	C ₁₁ H ₈ O ₂ S ₂ (236.31)	219° (EtOH)	Found: 55.70	3.47	27.20	
(17)	cis isomer has not been isolated						
(cis, trans)	(18)	C ₁₁ H ₇ O ₂ ClS ₂ (270.76)	214° (MeOH-H ₂ O)	Calcd.: 48.80 Found: 48.50	2.61 2.61	23.68 23.40	13.09 13.40
	(24), (25)	C ₁₁ H ₈ O ₂ S ₂ (236.31)	108-109° (Hexane-Ether)	Calcd.: 55.91 Found: 55.80	3.41 3.31	27.13 27.00	
(28)		C ₁₁ H ₈ O ₂ S ₂ (236.31)	182° (EtOH)	Found: 55.73	3.87	27.20	
(35)	cis isomer has not been isolated						
(cis, trans)	(36)	C ₁₁ H ₆ O ₂ Cl ₂ S ₂ (305.20)	215-216° (Chloroform)	Calcd.: 43.29 Found: 43.40	1.98 2.05	21.01 21.00	23.23 23.30
	(trans)						

Table 4_{VI} continued

Unsaturated bromo compd. (mixture of)	Carbonated products obtained	Molecular formula (M.W.)	Mp (solvent)	Analyses %			
				C	H	S	Cl
(<u>47</u>), (<u>48</u>)	(<u>50</u>)	$C_{11}H_7O_2ClS_2$ (270.76)	152° (EtOH-H ₂ O)	Calcd.: 48.80 Found: 49.40	2.61 2.65	23.68 23.30	13.09 12.90
	(<u>51</u>)	$C_{11}H_7O_2ClS_2$ (270.76)	204° (EtOH-H ₂ O)	Found: 49.20	2.74	23.50	13.20
Carbonations of the saturated* bromo compounds							
(<u>9</u>)	(<u>12</u>)	$C_{11}H_{10}O_2S_2$ (238.33)	176° (Chloroform)	Calcd.: 55.44 Found: 55.59	4.23 4.22	26.91 27.08	
(d- <u>9</u>)	(d- <u>12</u>)	$C_{11}H_9DO_2S_2$ (239.32)	176° (Chloroform)				
(<u>26</u>)	(<u>29</u>)	$C_{11}H_{10}O_2S_2$ (238.33)	134° (EtOH-H ₂ O)	Calcd.: 55.44 Found: 55.59	4.23 4.22	26.91 26.78	
(d- <u>26</u>)	(d- <u>29</u>)	$C_{11}H_9DO_2S_2$ (239.32)	135° (Aceton-Water)				
(<u>37</u>)	(<u>38</u>)	$C_{11}H_8O_2Cl_2S_2$ (307.22)	121° (MeOH)	Calcd.: 43.00 Found: 42.80	2.62 2.60	20.87 20.80	23.08 23.10

* For preparation and characteristics of these saturated bromo compounds, see No 2 in Section D.

Table 5_{VI}. Spectral data of the carboxylic acid derivatives of the dithienyl-ethylenes and -ethanes

Carboxylic acid No	CO stretching (cm ⁻¹)	Nmr (The numbering of the assignments follows the numbering in the nomenclature)
(10)	1670	δ (acetone-d ₆) 6.6 [d., 1, J = 12 Hz, (2-CH=C)], 6.8-7.0 [m., 2, (thiophene)], 7.0 [d., 1, J = 12 Hz (1-CH=C)], 7.3 [m., 2, (thiophene)], 7.6 [d., 1, J = 5.2 Hz (5-thiophene)].
(11)	1665	δ (acetone-d ₆) 7.3 [d., 1, J = 16.1 Hz, (2-CH=C)], 7.4 [m., 3, (2',3',5-thiophene)], 7.5 [d., 1, J = 5.1 Hz, (4-thiophene)], 7.7 [d., 1, J = 5.1 Hz, (5-thiophene)], 8.0 [d., 1, J = 16.1 Hz, (1-CH=C)].
(18)	1660	δ (acetone-d ₆) 7.3 [d., 1, J = 18 Hz, (2-CH=C)], 7.3-7.6 [m., 4, (thiophene)], 7.7 [d., 1, J = 18 Hz, (1-CH=C)].
(27)	1670	δ (acetone-d ₆) 6.5-8.3 (multiplet in which no first order assignment is possible).
(28)	1675	δ (acetone-d ₆) 7.1 [d., 1, J = 16.4 Hz, (2-CH=C)], 7.0-7.6 [m., 5, (thiophene)], 8.1 [d., 1, J = 16.4 Hz, (1-CH=C-)].
(36)	1685	δ (DMSO-d ₆) 6.9 [d., 1, J = 16.5 Hz, (2-CH=C)], 7.4 [s., 1, (4'-thiophene)], 7.7 [d. of d., 1, J = 0.6 Hz, J = 16.5 Hz, (1-CH=C)], 7.9 [d. of d., 1, J = 0.6 Hz, J = 3.4 Hz, (2-thiophene)], 8.3 [d., 1, J = 3.4 Hz, (5-thiophene)].

Table 5_{VI} continued

Carboxylic acid No	CO stretching (cm ⁻¹)	Nmr (The numbering of the assignments follows the numbering in the nomenclature)
(50)	1685	δ (DMSO-d ₆) 6.4 [d., 1, J = 11.5 Hz, (2-CH=C)], 6.6 [d., 1, J = 5.8 Hz, (4-thiophene)], 6.9 [d. of d., 1, J = 1 Hz, J = 11.5 Hz, (1-CH=C)], 7.2 [d. of d., 1, J = 1 Hz, J = 3.3 Hz, (2-thiophene)], 7.3 [d., J = 5.8 Hz, (5'-thiophene)], 8.3 [d., 1, J = 3.3 Hz, (5-thiophene)].
(51)	1700	δ (DMSO-d ₆) 7.0 [d., 1, J = 16.5 Hz, (2-CH=C)], 7.3 [d., 1, J = 5.8 Hz, (4'-thiophene)], 7.5 [d. of d., 1, J = 0.8 Hz, J = 5.8 Hz, (5'-thiophene)], 7.7 [d. of d., 1, J = 0.8 Hz, J = 16.5 Hz, (1-CH=C)], 7.9 [d. of d., 1, J = 0.8 Hz, J = 3.2 Hz, (2-thiophene)], 8.3 [d., 1, J = 3.2 Hz, (5-thiophene)].
(12)	1670	δ (DMSO-d ₆) 2.5-3.6 [m., 4, (-CH ₂ -CH ₂ -)], 7.0 [d. of d., 1, J = 1.4 Hz, J = 5 Hz, (4'-thiophene)], 7.0 [d., 1, J = 5 Hz (4-thiophene)], 7.1 [d. of t., 1, J = 1.4 Hz, J = 2.7 Hz, (2'-thiophene)], 7.4 [d. of d., 1, J = 2.7 Hz, J = 5 Hz, (5'-thiophene)], 7.7 [d., 1, J = 5 Hz, (5-thiophene)].
(d-12)	1670	δ (DMSO-d ₆) 2.5-3.6 [m., 4, (-CH ₂ -CH ₂ -)], 7.0 [d., 1, J = 5 Hz, (4-thiophene)], 7.1 [d., 1, J = 2.7 Hz, (2'-thiophene)], 7.4 [d., 1, J = 2.7 Hz, (5'-thiophene)], 7.7 [d., 1, J = 5 Hz, (5-thiophene)].

Table 5_{VI} continued

Carboxylic acid No	CO stretching (cm ⁻¹)	Nmr (The numbering of the assignments follows the numbering in the nomenclature)
(d-29)	1675	δ (acetone-d ₆) 3.0-3.8 [m., 4, (-CH ₂ -CH ₂ -)], 6.9 [s. (broad), 1, (3'-thiophene)], 7.2 [d. (broad), 1, J = 0.7 Hz, (5'-thiophene)], 7.2 [d., 1, J = 5.4 Hz, (4-thiophene)], 7.5 [d., 1, J = 5.4 Hz, (5-thiophene)].
(29)	1675	δ (acetone-d ₆) 3.0-3.8 [m., 4, (-CH ₂ -CH ₂ -)], 6.9 [d., 1, J = 4.4 Hz, (4'-thiophene)], 6.9 [m., 1, (3'-thiophene)], 7.2 [m., 1, J = 4.4 Hz, J = ?, (5'-thiophene)], 7.2 [d., 1, J = 5.4 Hz, (4-thiophene)], 7.4 [d., 1, J = 5.4 Hz, (5-thiophene)].
(38)	1690	δ (CDCl ₃) 2.8-3.2 [m., 4, (-CH ₂ -CH ₂ -)], 6.6 [s., 1, (4'-thiophene)], 6.9 [d., 1, J = 3.4 Hz, (2-thiophene)], 8.3 [d., 1, J = 3.4 Hz, (5-thiophene)], 11.5 [s., 1, (-C-OH)].

No 2. General procedure for the homogeneous hydrogenation of the 1,2-dithienylethylenes using T.T.Rh^ICl (Wilkinson catalyst) (41) as catalyst

0.1 mole of pure olefin (cis and trans mixture) was dissolved (or suspended as in the hydrogenation of (36) in 300 ml of ethanol. The solution (suspension) was degassed for five minutes by passing a rapid stream of dry nitrogen through it. 0.8 mg of Wilkinson catalyst was added to the solution, which was degassed again for another 3 minute period. The mixture was then hydrogenated in a Parr apparatus at 60-70° at a hydrogen pressure which varied between 60-30 PSI during the hydrogenation. Hydrogenation of the olefinic bond was complete when no more hydrogen was absorbed (20-30 hrs for carboxylic acids and 40-50 hrs for the bromo derivatives). The solution was concentrated.

If the olefin was a bromo derivative, the residue was chromatographed on a silica gel column with benzene as the eluent. The catalyst-free solution was concentrated, and then fractionated under reduced pressure. Yields of pure saturated products were 90-95 %.

For the bromo olefins, hydrogenated by this method, the products, and their physical characteristics, see Table 6_{VI}.

In case the product was a carboxylic acid derivative, the residue was dissolved in aq. NaOH, filtered (cotton) and then acidified. The saturated carboxylic acid, which was precipitated, was filtered after 2 hrs. Yields were greater than 95 %.

All the saturated carboxylic acids obtained by this method, as well as their physical data, are given in Table 7_{VI}.

Table 6_{VI}. Physical characteristics of the bromo-dithienyl-ethanes obtained from hydrogenation of the corresponding bromo-dithienyl-ethylene derivatives

Bromo olefin (mixture of)	Saturated product	B.P. (mm Hg)	n _D ²⁰	Analyses %	Nmr
(<u>7</u>), (<u>8</u>)	(<u>9</u>)	108-110° (7x10 ⁻³)	1.6208	Calcd. for C ₁₀ H ₉ BrS ₂ (M.W. 273.22) C 43.96; H 3.32; Br 29.25; S 23.47. Found: C 44.3; H 3.35; Br 29.30; S 23.70	(CDCl ₃): δ 2.8 [s., 4, (-CH ₂ -CH ₂ -)], 6.6 [d., 1, J=5.7 Hz, (4-thioph.)], 6.8 [d., 1, J=4.3 Hz, (4'-thioph.)], 6.8 [d. of d., 1, J=1.3 Hz, J=3 Hz, (2'-thioph.)], 7.0 [d., 1, J=5.7 Hz, (5-thioph.)], 7.1 [d. of d., 1. J=3 Hz, J=4.7 Hz, (5'-thioph.)].
(<u>d-7</u>), (<u>d-8</u>) (crude)	(<u>d-9</u>)	100-115° (5x10 ⁻³)	1.6208	-	(CDCl ₃): δ 2.8 [s., 4, (-CH ₂ -CH ₂ -)], 6.6 [d., 1, J=5.7 Hz, (4-thioph.)], 6.8 [d., 1, J=3 Hz, (2'-thioph.)], 7.0 [d., 1, J=5.7 Hz, (5-thioph.)], 7.1 [d., 1, J=3 Hz, (5'-thioph.)].

Table 6_{VI} continued

Bromo olefin (mixture of)	Saturated product	B.p. (mm Hg)	n _D ²⁰	Analyses %	Nmr
(<u>24</u>), (<u>25</u>)	(<u>26</u>)	110-115 ⁰ (1x10 ⁻²)	1.6205	Calcd. for C ₁₀ H ₉ BrS ₂ (M.W. 273.22) C 43.96; H 3.32; Br 29.25; S 23.47. Found: C 44.10; H 3.32; Br 29.20; S 24.00	(CDCl ₃): δ 3.1 [s., 4, (-CH ₂ -CH ₂ -)], 6.7, [m., 1, (4'-thioph.)], 6.8 [d., 1, J=5.2 Hz, (4- thioph.)], 6.9 [d. of d., 1, J=1.4 Hz, J=3.5 Hz, (3'-thioph.)], 7.0 [d., 1, J=5.2 Hz, (5-thioph.)], 7.1 [d. of d., 1, J=1.4 Hz, J=5Hz, (5'-thioph.)].
(<u>d-24</u>), (<u>d-25</u>) (crude)	(<u>d-26</u>)	105-110 ⁰ (5x10 ⁻³)	1.6204	-	(CDCl ₃): δ 3.1 [s., 4, (-CH ₂ -CH ₂ -)], 6.8 [d., 1, J=5.2 Hz, (4-thioph.)], 6.9 [d., 1, J=1.4 Hz, (3'-thioph.)], 7.0 [d., 1, J=5.2 Hz, (5-thioph.)], 7.1 [d., 1, J=1.4 Hz, (5'-thioph.)].

Table 6_{VI} continued

Bromo olefin (mixture of)	Saturated product	B.p. (mm Hg)	n_D^{20}	Analyses %	Nmr
(<u>35</u>) cis and trans	(<u>37</u>)	130-134° (1x10 ⁻²)	1.6280	Calcd. for C ₁₀ H ₇ BrCl ₂ S ₂ (M.W. 342.11) C 35.11; H 2.06; Hal (Cl) 31.09; S 18.74. Found: C 35.40; 1, J=3.3 Hz, (2-thioph.), H 2.13; Hal (Cl) 30.80; 7.2 [d., 1, J=3.3 Hz, (5-thioph.)]. S 19.00	(CDCl ₃): δ 2.8 [s., 4, (-CH ₂ -CH ₂ -)], 6.6 [s., 1, (4'-thioph.)], 6.9 [d., 1, J=3.3 Hz, (2-thioph.)], 7.2 [d., 1, J=3.3 Hz, (5-thioph.)].

Table 7_{VI}. Physical characteristics of the dithienyl-ethane carboxylic acid derivatives obtained from hydrogenation of the corresponding dithienyl-ethylene carboxylic acids

Unsaturated carboxylic acid (mixture of)	Saturated product	Mp (solvent)	Analyses %	Nmr and ir
(<u>10</u>), (<u>11</u>)	(<u>12</u>)		See Tables 4 _{VI} and 5 _{VI}	
(<u>18</u>) cis and trans	(<u>19</u>)	110-111° (EtOH-H ₂ O)	Calcd. for C ₁₁ H ₉ O ₂ ClS ₂ (M.W. 272.77) C 48.44; H 3.32; Cl 12.99; S 23.51. Found: C 48.20; 7.1 [s., 1, (4-thioph.)], 7.2 H 3.45; Cl 13.10; S 23.40	(DMSO-d ₆): δ 2.7-3.4 [m., 4, (-CH ₂ -CH ₂ -)], 7.0 [d. of d., 1, J=1.4 Hz, J=4.9 Hz, (4'-thioph.)], 7.2 [m., 1, (2'-thioph.)], 7.5 [d. of d., 1, J=3 Hz, J=4.9 Hz, (5-thioph.)], C-O stretching frequency 1675 cm ⁻¹ .
(<u>27</u>), (<u>28</u>)	(<u>29</u>)	-	See Tables 4 _{VI} and 5 _{VI}	
(<u>36</u>) cis and trans	(<u>38</u>)	-	See Tables 4 _{VI} and 5 _{VI}	

Table 7_{VI} continued

Unsaturated carboxylic acid (mixture of).	Saturated product	Mp (solvent)	Analyses %	Nmr and ir
(<u>50</u>), (<u>51</u>)	(<u>52</u>)	140° (EtOH-H ₂ O)	Calcd. for C ₁₁ H ₉ O ₂ ClS ₂ (M.W. 272.77) C 48.44; H 3.32; Cl 12.99; S 23.51. Found: C 48.70; J=3.3 Hz, (2-thioph.), 7.3 [d., H 3.45; Cl 13.00; S 23.20	(DMSO-d ₆): δ 2.6-3.3 [m., 4, (-CH ₂ -CH ₂ -)], 6.9 [d., 1, J=5.6 Hz, (4'-thioph.)], 7.1 [d., 1, (2-thioph.)], 7.3 [d., 1, J=5.3 Hz, (5'-thioph.)], 8.2 [d., 1, J=3.3 Hz, (5-thioph.)], C-O stretching frequency 1685 cm ⁻¹

Section E. Ketones

No 1. Friedel-Crafts-type cyclizations of 1-(carboxythienyl)-2-(thienyl) ethanes with tin tetrachloride as catalyst

General procedure. To a benzene solution of the carboxylic acid (0.01 mole/60-70 ml solvent), 1.2 equiv. of phosphorous pentachloride was added. The mixture was warmed for a few minutes on a hot water bath until all the solids were in solution, and then refluxed for another 10 minutes. After cooling, the solution was degassed by bubbling nitrogen through it for 15-20 min. The solution was cooled again to 5-6°, and an equivalent amount of tin tetrachloride in benzene was added quickly. The dark complex (yellow to black in colour) which formed, intensified with stirring. Efficient stirring was continued until the mixture reached room temperature. It was then heated on a water bath at about 90° for 10-12 min. It was cooled, and ether was added until a homogeneous solution of the complex was formed. The complex was cooled on an ice-bath and decomposed by 5 N aq. HCl (50 ml/0.01 mole), which was added through the condensor, followed by an equal amount of water. After a few minutes of efficient stirring the layers were separated. The aqueous layer was diluted with water and extracted with ether. The solid materials which remained (if any) were dissolved in acetone, poured onto 0.5 N aq. HCl and extracted with ether. The combined organic layers were washed three times with each of the following solutions: 5 N HCl, 3 N HCl, 1 N HCl, water 1 N NaOH and water, then dried (CaCl₂) and evaporated. The crude ketones were obtained in good yields and were reasonably pure.

All the ketones prepared by this general method, as well as their physical characteristics, are registered in Table 8_{VI}; for spectral data of these ketones see Table 9_{VI}.

Table 8_{VI}. List of the (dihydro)-cycloheptadithiophene-ones obtained from cyclization of the corresponding carboxylic acids (according to the procedure given in No 1) and their physical data

Carboxylic acids which were cyclized	Ketones obtained	Crude yield %	Mp (solvent)	Analyses %
(<u>12</u>)	(<u>13</u>)	94.4	105-106 ^o (MeOH)	Calcd. for C ₁₁ H ₈ OS ₂ (M.W. 220.31) C 59.96; H 3.66; S 29.10. Found: C 59.81; H 3.70; S 29.4
(d- <u>12</u>)	(d- <u>13</u>)	94.5	105-106 ^o (MeOH)	-
(<u>19</u>)	(<u>20</u>)	84.5	99-100 ^o (MeOH)	Calcd. for C ₁₁ H ₇ OCIS ₂ (M.W. 254.76) C 51.86; H 2.77; Cl 13.92; S 25.17. Found: C 51.90; H 2.82; Cl 14.10; S 25.10
(<u>29</u>)	(<u>30</u>)	93	95 ^o (MeOH)	Calcd. for C ₁₁ H ₈ OS ₂ (M.W. 220.31) C 59.96; H 3.66; S 29.10. Found: C 59.90; H 3.73; S 29.20
(<u>29</u>)	(<u>33</u>)*	82	109-110 ^o (MeOH)	Calcd. for C ₁₁ H ₇ OCIS ₂ (M.W. 254.76) C 51.86; H 2.77; Cl 13.92; S 25.17. Found: C 51.80; H 2.73; Cl 13.30; S 25.10

Table 8_{VI} continued

Carboxylic acids which were cyclized	Ketones obtained	Crude yield	Mp (solvent)	Analyses %
(<u>d-29</u>)	(<u>d-30</u>)	93	95° (MeOH)	
(<u>10</u>)	(<u>31</u>)	85	151-152° (CH ₃ CN)	Calcd. for C ₁₁ H ₆ OS ₂ (M.W. 218.30) C 60.52; H 2.77; S 29.38. Found: C 60.70; H 2.80 S 29.3
(<u>27</u>)	(<u>32</u>)	81	172-173° (CH ₃ CN)	Calcd. for C ₁₁ H ₆ OS ₂ (M.W. 218.30) C 60.52; H 2.77; S 29.38. Found: C 60.00; H 2.67; S 29.00
(<u>52</u>)	(<u>53</u>)**	81.5	96° (MeOH)	Calcd. for C ₁₁ H ₇ OCls ₂ (M.W. 254.76) C 51.86; H 2.77; Cl 13.92; S 25.17. Found: C 52.96; H 2.96; Cl 13.73; S 24.97

* This ketone was obtained when the unchlorinated carboxylic acid was treated with 3.0 equiv. of PCl₅ and the reaction mixture refluxed 2 hrs before adding SnCl₄ (see No 1 of Section E).

** In order to get good yields of this ketone, the reaction mixture should be refluxed for 90 minutes, instead of 10 min as stated in the procedure, after addition of the SnCl₄ solution, and before decomposition by HCl.

No 2. 1,3-Dichloro-8,9-dihydro-4H-cyclohepta[1,2-c;4,5-c']-dithiophen-4-one (39)

To a solution of 21.5 g (0.07 mole) of carboxylic acid (38) in 350 ml of dry benzene, 18.0 g of PCl_5 was added in portions. The mixture was warmed slowly to reflux, and was refluxed until the evolution of hydrochloric acid had nearly ceased. The solution obtained in this way was diluted with ether, washed with water until neutral, dried (Na_2SO_4) and concentrated. The oily residue was dissolved in 200 ml of dry carbon disulphide, and added dropwise to an ice-cooled suspension of 10 g of AlCl_3 in 150 ml of dry CS_2 , protected from moisture. The mixture was stirred 1 hr with cooling, overnight at room temperature, and then refluxed for 2 hrs. The reaction mixture was poured onto a mixture of 5 N HCl and crushed ice. After all the complex was decomposed, the organic layer was separated, and the water layer was extracted 2-3 times with ether. The combined organic phases were washed with 1 N HCl (5 times), water (3 times), 1 N KOH and water, dried (Na_2SO_4) and concentrated. If there is acid chloride left [ir (film): 1755 cm^{-1} (C-O)] the residue, an oil, should be boiled with 1 N KOH for 10 min, and then extracted with ether, dried, and concentrated again. The residue was further purified by extracting it with hexane. The soluble fraction was concentrated, and gave 16.2 g (80 %) of crude ketone which contained roughly 10 % of an unidentified isomeric ketone [ir (film): 1615 cm^{-1} (C-O)]. The main fraction however was (39); mp (hexane): 74° ; for spectral data see Table 9_{VI}. Calcd. for $\text{C}_{11}\text{H}_6\text{OCl}_2\text{S}_2$ (M.W. = 289.20): C 45.68; H 2.09; Cl 24.52; S 22.17. Found: C 46.00; H 2.19; Cl 24.70; S 22.10.

No 3. 8,9-Dihydro-4H-cyclopenta[1,2-c;4,5-c']-dithiophen-4-one (54)

1.6 g of the dichloro derivative (39) was refluxed with copper (4-5 g fine powder) in butyric acid, for 70 hrs, cooled and then filtered. The filter cake was washed with a small

amount of acetone. The dark blue filtrate was poured onto 400 ml cold water, and then extracted with ether. The ethereal layer was washed twice with water, 1 N KOH (three times) and finally with water until neutral. The resulting solution was dried (CaCl_2), decolourized, concentrated, and the oily residue dissolved in boiling acetonitrile. Yellow crystals, 0.85 g (71 %), of (54) were obtained when this solution was stored cold for a few days. The remainder contained (from nmr, ir) both the mono-chloro derivative (53) and (54). Mp (acetonitrile) 131° . For spectral data see Table 9_{VI}. Calcd. for $\text{C}_{11}\text{H}_8\text{OS}_2$ (M.W. = 220.313): C 59.96; H 3.66; S 29.1. Found: C 60.40; H 3.82; S 29.0.

No 4. Cycloheptadithiophene-ones from side-chain bromination, dehydrobromination of the corresponding dihydroprecursors

General procedure. 3.0 g (13.6 mmole) of the dihydrocyclohepta-dithiophene-one (unsubstituted) was dissolved in 75 ml of anhydrous carbon tetrachloride and an equivalent amount (2.4 g) of NBS mixed with 0.3-0.4 g of ABN was added. The mixture was stirred and refluxed. With b-annelated dihydro ketones an evolution of hydrobromic acid was apparent after 20 minutes. Refluxing was continued about 1.5 hrs and then another 50 ml-portion of carbon tetrachloride was added. The reaction mixture was cooled to room temperature and the succinimide was filtered. The filtrate was washed twice with water, dried (Na_2SO_4) and concentrated. The residue was dissolved in 100 ml of abs. methanol and 2-3 g sodium methoxide was added. The mixture was boiled for 0.5 hr, then concentrated to one half its volume and poured onto water. The insoluble organic materials were extracted with chloroform, washed until neutral, dried and concentrated. The residue was dissolved in boiling acetonitrile, and decolourized with norite. The products crystallized from the solutions when kept cool ($4-5^\circ$) for 1-2 days.

No 5. 9H-Cyclohepta[2,1-b;4,5-b']dithiophen-9-one (31), and
3-deutero-9H-cyclohepta[2,1-b;4,5-b']dithiophen-9-one

(d-31) were prepared from the saturated precursors (13) and (d-13) respectively, according to No 4. Yields were the same; 2.7 g (90 %) of unsaturated ketone was obtained in each case. Recrystallized from acetonitrile, (31) and (d-31) had the same melting points (see Table 8_{VI}). For spectral data see Table 9_{VI}.

No 6. 4H-Cyclohepta[1,2-b;5,4-b']dithiophen-4-one (32) and
3-deutero-4H-cyclohepta[1,2-b;5,4-b']dithiophen-4-one

(d-32) were obtained from the saturated ketones (30) and (d-30) respectively, according to No 4. In both cases similar yields, 2.5-2.6 g (83-86 %), were obtained. After recrystallization from acetonitrile, both ketones had the same melting point (see Table 8_{VI}). See Table 9_{VI} for spectral data.

No 7. 4H-Cyclohepta[2,1-c;4,5-c']dithiophen-4-one (80)

Side-chain bromination of the dithienocycloheptanone (54) by NBS followed by dehydrobromination, according to No 4 gave 2.1 g (70 %) of (80). Mp (acetonitrile) 160°.

Calcd. for C₁₁H₆OS₂ (M.W. = 218.30): C 60.52; H 2.77; S 29.38. Found: C 60.05; H 2.65; S 28.90. See Table 9_{VI} for spectral data.

Table 9_{VI}. Spectral data (uv, ir and nmr) for all the (dihydro)-cycloheptadithiophene-ones, the preparation of which was described in this section

Ketone	Uv (abs. EtOH), max... mμ(ε...)	Ir (KBr) (C=O)	Nmr (solvent)
(13)	328 (1.52x10 ⁴), 281 (1.07x10 ⁴), 218 (4.89x10 ³)	1595 cm ⁻¹	(CDCl ₃): δ 3.1 [s., 4, (-CH ₂ -CH ₂ -)], 6.9 [d., 2, J=5 Hz, (β-thioph.)], 7.5 [d., 2, J=5 Hz, (α-thioph.)].
(d-13)	-	1595 cm ⁻¹	(CDCl ₃): δ 3.1 [s., 4, (-CH ₂ -CH ₂ -)], 6.9 [d., 1, J=5 Hz, (β-thioph.)], 7.5 [d., 1, J=5 Hz, (α-thioph.)], 7.5 [s., 1, (α-thioph.)].
(20)	337 (1.85x10 ⁴), 280 (1.08x10 ⁴), 222 (5.21x10 ³)	1595 cm ⁻¹	(CDCl ₃): δ 3.1 [s., 4, (-CH ₂ -CH ₂ -)], 6.8 [s., 1, (β-thioph.)], 6.9 [d., 1, J=5 Hz, (β-thioph.)], 7.5 [d., 1, J=5 Hz, (α-thioph.)].
(30)	312 (2.77x10 ³), 264 (1.53x10 ⁴), 225 (1.56x10 ⁴)	1620 cm ⁻¹	(CS ₂): δ 3.3 [s., 4, (-CH ₂ -CH ₂ -)], 6.9 [d., 2, J=5.4 Hz, (α-thioph.)], 7.6 [d., 2, J=5.4 Hz, (β-thioph.)].
(d-30)	-	1620 cm ⁻¹	(CDCl ₃): δ 3.3 [s., 4, (-CH ₂ -CH ₂ -)], 7.0 [d., 1, J=5.5 Hz, (α-thioph.)], 7.0 [s., 1, (α-thioph.)], 7.7 [d., 1, J=5.5 Hz, (β-thioph.)].

Table 9_{VI} continued

Ketone	Uv (abs. EtOH), max... mμ (ε...)	Ir (KBr) (C=O)	Nmr (solvent)
(31)	370 (6.50x10 ³), 362 (6.50x10 ³), 350 (6.88x10 ³), 330 (7.26x10 ³), 289 (2.58x10 ⁴), 250 (2.52x10 ⁴)	1545 cm ⁻¹	(CDCl ₃): δ 7.4 [s., 2, (-CH=CH-)], 7.4 [d., 2, J=5.2 Hz, (β-thioph.)], 7.7 [d., 2, J=5.2 Hz, (α-thioph.)].
(d-31)	-	1545 cm ⁻¹	(CDCl ₃): δ 7.4 [s., 2, (-CH=CH-)], 7.4 [d., 1, J=5.2 Hz, (β-thioph.)], 7.7 [d., 1, J=5.2 Hz, (α-thioph.)], 7.7 [s., 1, (α-thioph.)].
(32)	373 (1.25x10 ⁴), 352 (1.60x10 ⁴), 337 (1.54x10 ⁴), 254 (3.09x10 ⁴)	1565 cm ⁻¹	(CDCl ₃): δ 7.2 [s., 2, (-CH=CH-)], 7.5 [d., 2, J=5.5 Hz, (α-thioph.)], 8.1 [d., 2, J=5.5 Hz, (β-thioph.)].
(d-32)	-	1565 cm ⁻¹	(CDCl ₃): δ 7.2 [s., 2, (-CH=CH-)], 7.5 [d., 1, J=5.5 Hz, (α-thioph.)], 7.5 [s., 1, (α-thioph.)], 8.1 [d., 1, J=5.5 Hz, (β-thioph.)].
(33)	315 (2.85x10 ³), 260.5 (1.71x10 ⁴), 231 (1.92x10 ⁴), 214 (1.17x10 ⁴)	1615 cm ⁻¹	(CS ₂): δ 3.2 [m., 4, (-CH ₂ -CH ₂ -)], 6.9 [d. of d., 1, J=5.4 Hz, J= 0.6 Hz, (α-thioph.)], 7.3 [s., 1, (β-thioph.)], 7.5 [d. of d., 1, J= 5.4 Hz, J=1.4 Hz, (β-thioph.)].

Table 9_{VI} continued

Ketone	Uv (abs. EtOH), max... mμ (ε...)	Ir (KBr) (C=O)	Nmr (solvent)
(39)	280 (1.90×10^4), 242 (1.13×10^4), 222 (1.37×10^4)	1632 cm^{-1} or 1647 cm^{-1}	(CDCl ₃): δ 3.0 [s., 4, (-CH ₂ -CH ₂ -)], 7.0 [d., 1, J=3.7 Hz, (7-posi- tion)], 8.4 [d., 1, J= 3.7 Hz, (5-position)].
(53)	280 (1.82×10^4), 221 (1.37×10^4)	1630 cm^{-1}	(CDCl ₃): δ 3.0 [s., 4, (-CH ₂ -CH ₂ -)], 7.0 [d., 2, J=3.6 Hz, (7-posi- tion)], 8.2 [s., 1, (3-position)], 8.4 [d., 1, J=3.6 Hz, (5-posi- tion)].
(54)	284 (1.97×10^4), 219 (1.52×10^4)	1620 cm^{-1}	(CDCl ₃): δ 3.0 [s., 4, (-CH ₂ -CH ₂ -)], 6.9 [d., 2, J=3.8 Hz, (1&7-posi- tions)], 8.4 [d., 2, J= 3.8 Hz, (3&5-positions)].
(80)	380 (4.48×10^2), 311 (2.83×10^3), 295 (3.58×10^3), 269.5 (1.42×10^4), 264 (1.30×10^4), 250 (1.00×10^4)	1618 cm^{-1}	(CDCl ₃): δ 6.7 [s., 2, (-CH=CH-)], 7.4 [d., 2, J=4 Hz, (thioph.)], 8.6 [d., 2, J=4 Hz, (thioph.)].

Section F. Cycloheptadithiophenes and dithienotropylium ions

No 1. 9H-Cyclohepta[2,1-b;4,5-b']dithiophene (81) and the
3-deutero derivative (d-81)

A mixture of 1.5 g (6.9 mmole) of the corresponding ketone (31) or (d-31) and 0.5 g of LiAlH_4 was suspended in 100 ml of abs. ether, and was stirred over night at room temperature, while protected from moisture. The excess of the metal hydride was decomposed by adding 90 % MeOH (ice-bath cooling) in small portions through the condenser. The reaction mixture was finally poured onto 200 ml of 1 N aq. HCl and stirred until all the solids were dissolved. The layers were separated and the aqueous layer was extracted with portions of ether (2 x 100 ml). The combined ethereal layers were washed with water, dried (CaCl_2) and evaporated to give pure (81) or (d-81) in quantitative yield, 1.4 g. The product was sensitive to light. For (81): mp (hexane) 98-99°. Uv max (cyclohexane 210 sh μ (ϵ 1.45×10^4), 233.5 μ (ϵ 3.2×10^4), 299 μ (ϵ 6.91×10^3). Nmr (CDCl_3): δ 4.0 [s., 2, ($-\text{CH}_2-$)], 6.7 [s., 2, ($-\text{CH}=\text{CH}-$)], 6.8 [d., 2, $J=5.1$ Hz, (β -thiophene)], 7.0 [d., 2, $J=5.1$ Hz, (α -thiophene)], for (d-81): nmr (CDCl_3): δ 4.0 [s., 2, ($-\text{CH}_2-$)], 6.7 [s., 2, ($-\text{CH}=\text{CH}-$)], 6.8 [d., 1, $J=5.1$ Hz (β -thiophene)], 7.0 [d., 1, $J=5.1$ Hz, (α -thiophene)], 7.0 [s., 1, (α -thiophene)]. Calcd. for $\text{C}_{11}\text{H}_8\text{S}_2$ (M.W. 204.32): C 64.66; H 3.94; S 31.39. Found: C 64.30; H 3.87; S 31.10.

No 2. 4H-Cyclohepta[1,2-b;5,4-b']dithiophene (82) and its
3-deutero derivative (d-82)

These compounds were obtained by reducing the ketones (30) and (d-30) respectively with LiAlH_4 in anhydrous ether, according to the procedure used for (81) (No 1, of this section). This gave (82) and (d-82) nearly quantitatively. For (82): mp (hexane) 132-133°. Uv max (cyclohexane) 208.5 μ (ϵ 9.34×10^3), 245 μ (ϵ 9.32×10^3); 267 sh. μ (ϵ 8.37×10^3); 332.5 μ (ϵ 1.34×10^4). Nmr (CDCl_3): δ 3.8 [s., 2, ($-\text{CH}_2-$)], 6.7 [s., 2, ($-\text{CH}=\text{CH}-$)], 6.8 [d., 2,

J=5 Hz, (β -thiophene)], 7.2 [d., 2, J=5 Hz, (α -thiophene)].
 For (d-82): nmr (CDCl_3): δ 3.8 [s., 2, ($-\text{CH}_2-$)], 6.7 [s., 2, ($-\text{CH}=\text{CH}-$)], 6.8 [d., 1, J=5 Hz, (β -thiophene)], 7.2 [d., 1, J=5 Hz, (α -thiophene)], 7.2 [s., 1, (α -thiophene)].
 Calcd. for $\text{C}_{11}\text{H}_8\text{S}_2$ (M.W. 204.32): C 64.66; H 3.94; S 31.39.
 Found: C 64.20; H 4.01; S 31.20.

No 3. 9H-Dithieno-[2,1-b;4,5-b']tropylium perchlorate (84)
and its 3-deutero derivative (d-84)

To a solution of 0.20 g (1 mmole) of the corresponding hydrocarbon (81) or (d-81) in 25 ml of dry EtOAc, 0.6 g of trityl perchlorate dissolved in 10 ml of acetonitrile was added dropwise. An instant yellow precipitate was formed. After all the trityl perchlorate was added, the suspension was stirred an additional 15 min at room temperature and stored for 2 hrs in the cold. The yellow precipitate was filtered, washed with ether and dried, giving 0.3 g (99 %) of the corresponding tropylium ion.

The pK_R^+ value of the carbonium ion was determined by potentiometric titration of 1.68×10^{-4} M of (84) with 9.91×10^{-3} N NaOH in aqueous solutions, at 25° . Taking the pH value at the half-way point on the titration curve, a pK_R^+ value of 6.65 ± 0.05 was obtained.

For (84): Mp (acetonitrile) 288° . Uv max (H_2SO_4 97 %) 208 m μ (ϵ 1.74×10^4), 235 m μ (ϵ 1.46×10^4), 265.5 m μ (ϵ 8.42×10^3), 301.5 m μ (ϵ 3.75×10^4), 330.5 m μ (ϵ 4.62×10^4), 375 m μ (ϵ 7.25×10^3), 395 m μ (ϵ 1.57×10^4), 447 m μ (ϵ 4.65×10^3), 460.5 m μ (ϵ 5.0×10^3), 471 m μ (ϵ 4.68×10^3).
 Nmr (H_2SO_4): δ 8.7 [d., 2, J=5.5 Hz, (β -thiophene)], 9.4 [d., 2, J=5.5 Hz, (α -thiophene)], 9.4 [s., 2, ($-\text{CH}=\text{CH}-$)], 10.3 [s., 1, ($-\overset{+}{\text{CH}}-$)].

Calcd. for $\text{C}_{11}\text{H}_7\text{S}_2\text{ClO}_4$ (M.W. 302.77): C 43.63; H 2.33; S 21.18.
 Found: C 43.70; H 2.24; S 21.20.

For (d-84): Nmr (H_2SO_4): δ 8.7 [d., 1, J=5.5 Hz, (β -thiophene)], 9.4 [d., 1, J=5.5 Hz, (α -thiophene)], 9.4 [s., 1, (α -thiophene)], 9.4 [s., 2, ($-\text{CH}=\text{CH}-$)], 10.3 [s., 1, ($-\overset{+}{\text{CH}}-$)].

No 4. 4H-Dithieno[1,2-b;5,4-b']tropylium perchlorate (85)
and its 3-deutero derivative (d-85)

These compounds were obtained in nearly quantitative yields from (82) and (d-82) according to the method outlined in No 3 above.

The pK_R^+ value of (85) was determined in a similar way as for (84). A 1.935×10^{-4} M aq. solution of (85) was titrated with the 9.91×10^{-3} N NaOH solution, at 25° , and gave a pK_R^+ value of 5.4 ± 0.05 .

For (85): Mp (acetonitrile) 310° . Uv max (H_2SO_4 97 %), 205 m μ (ϵ 1.77×10^4), 223 m μ (ϵ 1.77×10^4), 230 (sh) m μ (ϵ 1.55×10^4), 312 m μ (ϵ 8.09×10^4), 374 m μ (ϵ 6.0×10^3), 411 m μ (ϵ 7.7×10^3), 440 (sh) m μ (ϵ 2.88×10^3), 470 (sh) m μ (ϵ 1.11×10^3). Nmr (H_2SO_4): δ 8.7 [d., 2, $J=5.5$ Hz, (β -thiophene)], 9.0 [d., 2, $J=5.5$ Hz, (α -thiophene)], 9.6 [s., 2, ($-CH=CH-$)], 10.3 [s., 1, ($-CH-$)].

For (d-85): Nmr (H_2SO_4): δ 8.7 [d., 1, $J=5.5$ Hz, (β -thiophene)], 9.0 [d., 1, $J=5.5$ Hz, (α -thiophene)], 9.0 [s., 1, (α -thiophene)], 9.6 [s., 2, ($-CH=CH-$)], 10.3 [s., 1, ($-CH-$)].
Calcd. for $C_{11}H_7S_2.ClO_4$ (M.W. 302.77): C 43.63; H 2.33; S 21.18.
Found: C 43.80; H 2.17; S 21.10.

Section G. 3-N-Methylamino-propylidene derivatives of the dihydrocycloheptadithiophenes

No 1. Preparation of 3-N,N-dimethylaminopropyldihydrocycloheptadithiophene-oles

General procedure. To 25 ml of a ca. 1.75 N solution of 3-dimethylaminopropylmagnesium chloride in THF prepared in the usual manner (18), a solution of 25 mmole of the dihydrocycloheptadithiophene-one in 50 ml of anhydrous THF was added dropwise, under N_2 and protected from moisture. After adding all the solution (10 min), the mixture was stirred another 15 min at room temperature and then refluxed for 30 min. It was cooled, concentrated to half its volume and poured onto 250 ml 20 % ammonium chloride solution in water. The organic substances were extracted with 3 x 150 ml portions of ether. The combined ethereal layers were washed with water, dried ($CaCl_2$) and evaporated. The products obtained in this manner were recrystallized from 60-75° petroleum ether (P.E.).

No 2. 9-(3-Dimethylaminopropyl)-4,5-dihydro-9H-cyclohepta[2,1-b;4,5-b']dithiophen-9-ol (88)

This compound was obtained from the reaction between (13) and 3-dimethylaminopropylmagnesium chloride according to the general procedure No 1. The yield was 86-87 %. Mp (P.E., 60-75°) 120°.

Calcd. for $C_{16}H_{21}ONS_2$ (M.W. = 307.48): C 62.50; H 6.88; N 4.55; S 20.85. Found: C 63.32; H 6.95; N 4.70; S 20.85.

No 3. 2-Chloro-9-(3-dimethylaminopropyl)-4,5-dihydro-9H-cyclohepta[2,1-b;4,5-b']dithiophen-9-ol (89)

This compound was obtained by reaction of (20) with 3-dimethylaminopropylmagnesium chloride, according to the general procedure No 1. Yield of crystalline product was 90 %. Mp (P.E.

60-75°) 119°.

Calcd. for $C_{16}H_{20}OClNS_2$ (M.W. 341.92): C 56.20; H 5.90; Cl 10.37; N 4.10; S 18.75. Found: C 56.20; H 5.80; Cl 10.30; N 4.13; S 18.80.

No 4. 4-(3-Dimethylaminopropyl)-8,9-dihydro-4H-cyclohepta-[1,2-b;5,4-b']dithiophen-4-ol (90)

This compound was obtained in 93 % yield when (30) was reacted with 3-dimethylaminopropylmagnesium chloride according to the procedure in No 1. Mp (P.E. 60-75°) 78°.

Calcd. for $C_{16}H_{21}ONS_2$ (M.W. 307.48): C 62.50; H 6.88; N 4.55; S 20.85. Found: C 62.58; H 6.20; N 4.87; S 21.10.

No 5. 1,3-Dichloro-4-(3-dimethylaminopropyl)-8,9-dihydro-4H-cyclohepta[1,2-c;4,5-c']dithiophen-4-ol (91)

The compound was obtained in 85 % yield in reaction of (39) with 3-dimethylaminopropylmagnesium chloride, according to the general procedure in No 1. Mp (hexane) 122°.

Calcd. for $C_{16}H_{19}Cl_2ONS_2$ (M.W. 376.37): C 51.06; H 5.22; Cl 18.82; N 3.72; S 17.04. Found: C 51.40; H 5.29; Cl 18.70; N 3.74; S 17.00.

No 6. 9-(3-Dimethylaminopropyliden)-4,5-dihydro-9H-cyclohepta-[2,1-b;4,5-b']dithiophene (92)

To a solution of 6.1 g (0.02 mole) of (88) in 80 ml of abs. ethanol, 20 ml of 7 N ethanolic solution of HCl was added. The clear solution thus obtained was stirred for about 30 min at room temperature and was boiled for 10 min. It was cooled, concentrated to 30 ml, and poured onto 150 ml cold water. The clear water solution was treated with a dilute solution of KOH until the pH reached 10-11 and the free amine was extracted with ether. The ether solution was washed with water several times, dried ($MgSO_4$) and concentrated, to give 4.6 g (80 %) of pure (92) in oily form, which could be obtained in crystalline form by dissolving in hexane and cooling in dry ice.

Mp (hexane, -70°) 41° . Nmr (CS_2): δ 2.1 [s., 6, ($-\text{N} \begin{smallmatrix} \text{CH}_3 \\ \diagup \end{smallmatrix}$)], 2.3-2.7 [m., 4, ($-\text{CH}_2-\text{CH}_2-\text{N} \begin{smallmatrix} \text{CH}_3 \\ \diagup \end{smallmatrix}$)], 2.8 [s., 4, ($-\text{CH}_2-\text{CH}_2-$)], 6.1 [m., 1, ($=\text{CH}-$)], 6.6 [d., 1, $J=5.1$ Hz, (β -thiophene)], 6.7 [d., 1, $J=5.1$ Hz, (β' -thiophene)], 6.8 [d., 1, $J=5$ Hz, (α -thiophene)], 7.0 [d., 1, $J=5$ Hz, (α' -thiophene)].
 Calcd. for $\text{C}_{16}\text{H}_{14}\text{NS}_2$ (M.W. 289.46): C 66.39; H 6.62; S 22.15; N 4.84. Found: C 66.60; H 6.71; S 22.2; N 4.86.

No 7. 2-Chloro-9-(3-dimethylaminopropyliden)-4,5-dihydro-9H-cyclohepta[2,1-b;4,5-b']dithiophene (93)

An ethanolic solution of (89) was treated with hydrochloric acid in the same way as in the dehydration of (90) in No 6. Compound (93) was obtained as an oily isomeric mixture (see nmr below) in 92 % yield. The ratio of the two isomers (a) and (b) was roughly estimated from nmr to be (a):(b) = 40:60.

Oil (isomeric mixture) nmr (CDCl_3): δ 2.2 [s., 6, ($-\text{N} \begin{smallmatrix} \text{CH}_3 \\ \diagup \end{smallmatrix}$)], 2.6 [m., 4, ($-\text{CH}_2-\text{CH}_2-\text{N} \begin{smallmatrix} \text{CH}_3 \\ \diagup \end{smallmatrix}$)], 2.9 [s., 4, ($-\text{CH}_2-\text{CH}_2-$)].

Isomer (a): 6.2 [t., 0.4, ($=\text{CH}-$)], 6.7 [s., 0.4, (β -thiophene)], 6.7 [d., 0.4, $J=5.4$ Hz, (β -thiophene)], 6.9 [d., 0.4, $J=5.4$ Hz, (α -thiophene)].

Isomer (b): 6.0 [t., 0.6, ($=\text{CH}-$)], 6.5 [s., 0.6, (β -thiophene)], 6.8 [d., 0.6, $J=5.2$ Hz, (β -thiophene)], 7.1 [d., 0.6, $J=5.2$ Hz, (α -thiophene)].

Calcd. for $\text{C}_{16}\text{H}_{18}\text{ClNS}_2$ (M.W. 323.91): C 59.33; H 5.60; Cl 10.94; N 4.32; S 19.80. Found: C 59.60; H 5.87; Cl 10.50; N 4.23; S 19.50.

No 8. 4-(3-Dimethylaminopropyliden)-8,9-dihydro-4H-cyclohepta[1,2-b;5,4-b']dithiophene (94)

Compound (94) was obtained by dehydration of (90) in a procedure similar to that described in No 6 for dehydration of (88). The yield of (94) was 82 %. Mp (hexane, -70°) 47° .

Nmr (CDCl_3): δ 2.2 [s., 6, ($-\text{N} \begin{smallmatrix} \text{CH}_3 \\ \diagup \end{smallmatrix}$)], 2.4 [m., 4, ($-\text{CH}_2-\text{CH}_2-\text{N} \begin{smallmatrix} \text{CH}_3 \\ \diagup \end{smallmatrix}$)], 3.1 [s., 4, ($-\text{CH}_2-\text{CH}_2-$)], 6.2 [t., 1, ($=\text{CH}-$)], 7.0 [m., 4, (thiophene)].

Calcd. for $C_{16}H_{19}NS_2$ (M.W. 289.46): C 63.39; H 6.62; S 22.15; N 4.84. Found: C 66.5; H 6.63; S 22.30; N 4.85.

No 9. 1,3-Dichloro-4-(3-dimethylaminopropyliden)-8,9-dihydro-4H-cyclohepta[1,2-c;4,5-c']dithiophene (95)

This compound was obtained by dehydration of (91), according to the procedure described in No 6 for dehydration of (88). The dehydrated product (95) was obtained in 93 % yield, as an oily substance consisting of two isomeric forms (a) and (b). A rough estimation of the isomeric ratio made from an nmr analysis of the mixture gave (a):(b) = 40:60. The isomers were not separated. Nmr ($CDCl_3$): δ 2.2 [s., 6, ($-N\langle CH_3$)], 2.5 [m., 4, ($-CH_2-CH_2-N\langle$)], 2.9 [m., 4, ($-CH_2-CH_2-$)], 6.1 [m., 1, ($=CH-$)].

Isomer (a): 6.9 [d., 0.4, $J=3$ Hz, (thiophene)], 7.0 [d., 0.4, $J=3$ Hz, (thiophene)].

Isomer (b): 7.2 [m., 1.2, (thiophene)].

Calcd. for $C_{16}H_{17}Cl_2NS_2$ (M.W. 358.35): C 53.63; H 4.78; Cl 19.79; S 17.90; N 3.91. Found: C 53.70; H 5.56; Cl 19.30; S 17.9; N 3.99.

No 10. 9-(3-Methylaminopropyliden)-4,5-dihydro-9H-cyclohepta-[2,1-b;4,5-b']dithiophene (100)

To a solution of 5.8 g (0.02 mole) of dimethylamino derivative (92) in 100 ml of benzene, a benzene (50 ml) solution of 6.5 g ethyl chloroformate was added dropwise (15 min). A solid intermediate which was formed during the addition decomposed slowly on stirring. The reaction mixture was stirred 24 hrs at room temperature, refluxed for 2 hrs and then cooled. The undecomposed solids were filtered. The filtrate was washed with 2 N aq. HCl, (3 x 60 ml portions) and water until neutral, dried ($MgSO_4$) and concentrated. The oily residue, presumably the carbamate (96), [ν 1700 cm^{-1} (C=O)] was dissolved in 80 ml of n-butanol, and was refluxed with 10 g of KOH for 6-7 hrs. After cooling, the solvent was evaporated, and 200 ml of benzene and 200 ml of water were added to the residue, shaken and the layers were separated. The organic phase was washed with water until neutral, and then extracted with 2 N aq. D-tartaric acid (3 x 70 ml portions). The pH of the combined aqueous layers was

adjusted to ≈ 10 by careful addition of alkali. The liberated free amine was extracted with ether (2-3 x 100 ml portions). The combined ethereal layers were washed with water until neutral, dried (MgSO_4) and concentrated to give an oily residue. The mono methyl derivative (100) was crystallized when its hexane solution was cooled at -70° over night to give 3.3 g, 60 %, of pure substance.

The hydrochloride was prepared by adding a dilute ethereal solution of HCl to a dilute ethereal solution of (100).

Hydrochloride: Mp (EtOH-acetone $234-236^\circ$ (dec.).

Nmr ($\text{DMSO}-d_6$): δ 2.5 [s., 4, ($-\text{CH}_2-\text{CH}_2-$)], 2.9 [m., 8, ($-\text{CH}_2-\text{CH}_2-\text{N} \begin{smallmatrix} \text{CH}_3 \\ \diagup \end{smallmatrix}$)], 6.1 [t., 1, ($=\text{CH}-$)], 6.8 [d., 1, $J=5.1$ Hz, (β -thiophene)], 7.0 [d., 1, $J=5$ Hz, (β -thiophene)], 7.2 [d., 1, $J=5.1$ Hz, (α -thiophene)], 7.5 [d., 1, $J=5$ Hz, (α -thiophene)]. Calcd. for $\text{C}_{15}\text{H}_{17}\text{NS}_2\cdot\text{HCl}$ (M.W. 311.90): C 57.56; H 5.82; Cl 11.37; N 4.49; S 20.56. Found: C 57.40; H 5.58; Cl 11.50; N 4.46; S 20.50.

No 11. 4-(3-Methylaminopropyliden)-8,9-dihydro-4H-cyclohepta-[1,2-b;5,4-b']dithiophene (101)

Procedure No 10 was repeated for 5.8 g (0.02 mole) of (94), giving 3.7 g (67 %) of the monomethyl derivative (101) via the ethyl carbamate intermediate (98).

Hydrochloride: Mp (EtOH-acetone) $245-247^\circ$ (decomp.).

Nmr (CDCl_3), free amine: δ 1.3 [d. of t., 2, $J=2.8$ Hz, $J=6.9$ Hz, ($=\text{CH}_2-\dot{\text{C}}-\text{N} \begin{smallmatrix} \diagup \end{smallmatrix}$)], 1.8-4.3 [m., 10, (aliphatic)], 6.0 [t., 1, ($=\text{CH}-$)], 7.0 [m., 4, (thiophene)].

Calcd. for $\text{C}_{15}\text{H}_{17}\text{NS}_2\cdot\text{HCl}$ (M.W. 311.90): C 57.76; H 5.82; Cl 11.37; N 4.49; S 20.56. Found: C 57.30; H 6.21; Cl 11.50; N 4.59; S 20.50.

APPENDIX

The Mass Spectra of Some
of the New Compounds

Mass spectra of the new compounds

Compound No	Fragments, m/e (%)
(<u>1</u>)	39(15.6), 45(10.8), 53(4.6), 83(10.0), 97(9.2), 111(100), 112(6), 113(4.4), 208(8.8).
(<u>2</u>)	29(5.4), 39(14.1), 41(8.3), 45(37.2), 51(4.5), 58(5.5), 59(3.8), 69(3.5), 81(7.6), 83(5.4), 84(3.1), 85(100), 86(6.4), 87(4.5), 97(10.4), 111(13.8), 112(4.1), 113(65.5), 114(100), 115(9.0), 116(4.8), 179(3.5).

1,2-Di-(3-thienyl)ethylenes

a) Halogen derivatives

(<u>8</u>)	39(5.2), 45(12.3), 63(6.2), 69(8.7), 77(3.0), 82(5.2), 89(3.0), 93(3.3), 95(18.0), 96(3.8), 102(3.9), 114(3.3), 121(6.1), 145(7.3), 146(4.1), 147(55.6), 148(6.8), 149(3.1), 158(6.7), 189(4.4), 190(54.8), 191(100), 192(21.3), 193(10.3), 270(21.8), 271(3.3), 272(23.2), 273(3.1).
(XLIII) cis,trans	45(5.6), 63(3.3), 69(6.6), 82(4.7), 93(3.3), 95(12.7), 120(3.8), 145(10.6), 146(5.6), 189(3.3), 190(100), 191(13.6), 192(10.0), 269(4.2), 270(3.3), 271(4.2), 348(7.5), 350(15.0), 352(8.4).
(<u>18</u>)	37(4.2), 38(5.5), 39(11.0), 45(39.0), 47(3.8), 49(3.0), 50(8.2), 51(6.0), 57(8.8), 58(8.8), 60(3.1), 61(5.7), 62(9.1), 63(9.9), 69(24.8), 70(3.5), 71(3.1), 73(4.0), 74(6.3), 75(5.0), 79(8.0), 81(11.4), 82(9.4), 84(3.5), 85(3.0), 86(4.1), 87(4.1), 89(3.0), 93(12.6), 94(4.1), 95(14.2), 96(3.1), 97(4.1), 102(5.0), 106(4.4),

Compound No	Fragments, m/e (%)
(18) continued	108(3.8), 117(4.4), 119(4.4), 120(3.5), 121(6.5), 123(3.1), 132(4.9), 145(23.1), 146(8.2), 181(7.5), 189(6.0), 190(100), 191(15.7), 192(12.3), 224(8.8), 225(16.4), 226(5.7), 227(7.2), 260(4.1), 262(4.1), 304(7.2), 306(10.4), 308(4.1).
(35)	45(7.6), 63(3.8), 69(6.6), 79(3.5), 81(4.1), 82(3.0), 93(4.1), 94(4.7), 112(14.7), 113(6.8), 144(3.6), 145(11.2), 179(5.5), 188(3.3), 189(9.6), 224(100), 225(15.8), 226(43.7), 227(6.0), 228(4.1), 268(10.7), 270(11.8), 302(7.1), 303(5.7), 304(10.4), 305(7.9), 306(4.1), 338(13.7), 340(22.4), 341(3.3), 342(12.0).
(48)	45(7.4), 63(3.5), 69(5.1), 82(3.2), 95(12.7), 145(8.7), 146(3.8), 158(3.0), 189(3.1), 190(100), 191(13.2), 192(10.7), 268(5.5), 269(5.3), 270(6.6), 271(5.6), 304(11.8), 306(16.0), 308(5.3).
b) <u>Carboxylic acid derivatives</u>	
(10), (11)	39(8.7), 44(4.0), 45(21.8), 50(3.3), 51(4.7), 58(4.0), 62(3.3), 63(8.7), 69(11.3), 74(3.3), 77(4.7), 82(5.3), 83(3.3), 84(3.3), 89(4.0), 92(4.0), 94(9.3), 95(4.0), 96(9.3), 102(4.7), 108(3.3), 111(8.0), 114(4.0), 115(3.3), 121(7.3), 134(4.0), 135(4.0), 139(5.3), 145(10.6), 146(5.3), 147(43.3), 148(5.3), 158(6.0), 159(3.3), 189(5.3), 190(42.6), 191(100), 192(20.6), 193(10.6), 203(13.3), 236(69.0), 237(10.0), 238(8.0).
(36)	26(4.6), 27(4.6), 28(9.3), 29(4.6), 32(4.6), 34(3.5), 35(4.6), 36(14.0), 37(4.6), 38(8.1), 39(9.3), 41(7.0), 42(3.5), 43(4.6), 44(7.0), 45(37.2), 46(4.6), 50(7.0), 51(4.6), 53(4.6), 55(4.6), 56(4.6), 57(7.0), 58(4.6), 60(3.5), 61(7.0), 62(7.0), 63(8.1), 65(3.5), 69(16.3), 70(4.6), 71(4.6), 72(4.6), 73(5.8), 74(7.0), 75(7.0), 76(4.6), 77(4.6), 79(11.6), 80(5.8), 81(11.6), 82(9.3), 83(7.0), 84(4.6), 85(4.6).

Compound No	Fragments, m/e (%)
(36)	86(4.6), 87(8.1), 89(7.0), 91(3.5), 93(9.3), 94(7.0),
continued	95(7.0), 96(4.6), 97(4.6), 98(4.6), 99(4.6), 101(4.6), 103(4.6), 105(3.5), 106(4.6), 107(4.6), 108(4.6), 109(4.6), 110(4.6), 111(8.1), 112(7.0), 113(7.0), 114(3.5), 117(5.8), 118(4.6), 119(4.6), 120(4.6), 121(4.6), 123(3.5), 125(4.6), 126(4.6), 129(4.6), 131(3.5), 132(4.6), 133(4.6), 134(3.5), 135(4.6), 139(8.1), 141(4.6), 142(3.5), 143(4.6), 144(7.0), 145(14.0), 146(4.6), 147(3.5), 152(5.8), 153(4.6), 145(3.5), 155(4.6), 156(4.6), 177(4.6), 178(4.6), 179(11.6), 181(9.2), 188(8.1), 189(9.2), 190(100), 191(16.3), 192(11.6), 193(3.5), 194(3.5), 205(4.6), 206(5.8), 207(4.6), 208(3.5), 213(4.6), 215(4.6), 216(3.5), 217(5.8), 222(3.5), 223(10.5), 224(20.9), 225(18.6), 226(12.8), 227(7.0), 228(4.6), 235(5.8), 236(4.6), 251(27.8), 252(8.1), 253(11.6), 254(4.6), 268(14.0), 269(21.0), 270(7.0), 271(10.5), 272(3.5), 304(24.4), 305(4.6), 306(21.0), 307(4.6), 308(7.0).
(50)	38(3.2), 39(7.5), 45(24.5), 50(5.3), 51(4.2), 58(3.2), 62(5.3), 63(10.5), 69(14.0), 73(4.3), 74(4.3), 75(4.3), 79(3.2), 81(5.3), 82(8.5), 83(4.3), 86(3.2), 87(4.3), 89(5.3), 91(3.2), 93(6.4), 94(3.2), 95(11.0), 96(3.2), 97(3.2), 101(3.2), 102(4.3), 108(3.2), 109(3.2), 111(3.2), 114(3.2), 117(3.2), 119(3.2), 120(3.2), 121(4.3), 133(3.2), 134(3.7), 135(4.3), 139(6.4), 144(3.2), 145(26.6), 146(8.0), 147(56.0), 148(7.5), 149(3.2), 158(6.4), 177(3.2), 179(6.4), 181(3.2), 188(3.2), 189(23.2), 190(64.0), 191(100), 192(19.2), 193(10.6), 217(45.0), 218(8.5), 219(4.3), 224(3.2), 234(17.0), 235(35.0), 236(8.5), 237(4.2), 270(34.0), 271(5.3), 272(15).
(51)	28(7.7), 36(5.3), 38(4.1), 39(9.4), 44(5.3), 45(28.3), 50(4.1), 51(4.7), 53(3.2), 62(4.7), 63(10.6), 69(13.0), 73(5.0), 74(3.8), 75(4.1), 79(3.5), 81(5.3), 82(7.1), 83(4.1), 85(4.1),

Compound No	Fragments, m/e (%)
(51)	86(4.1), 87(5.3), 89(4.7), 93(4.7), 94(3.5),
continued	95(13.5), 96(3.5), 97(4.7), 102(3.5), 109(4.1),
	111(3.5), 114(3.3), 121(3.5), 131(18.3), 132(3.5),
	133(9.4), 134(4.1), 135(8.2), 139(7.7), 141(7.4),
	145(20.6), 146(5.9), 147(50.0), 148(5.9), 158(4.7),
	177(3.2), 189(20.0), 190(56.0), 191(100), 192(18.2),
	193(11.2), 217(44.2), 218(8.2), 219(5.9), 234(15.9),
	235(37.1), 236(11.8), 237(10.6), 270(51.8),
	271(8.2), 272(23.5), 273(3.5).

c) Other derivatives

(59)	15(3.6), 16(3.4), 26(5.6), 27(20.2), 28(21.2),
	29(59.5), 31(8.7), 32(3.0), 39(34.0), 40(3.8),
	41(72.3), 42(5.9), 43(8.3), 45(36.1), 47(3.0),
	51(10.0), 52(3.8), 53(14.7), 54(3.0), 55(10.0),
	56(5.5), 57(100), 58(8.5), 59(13.4), 63(9.3),
	64(3.4), 65(12.1), 67(5.9), 69(8.9), 70(3.1),
	71(7.1), 74(4.4), 75(4.0), 76(3.0), 77(21.4),
	78(5.5), 79(9.5), 83(4.4), 84(6.5), 85(10.0),
	87(3.6), 89(8.1), 90(3.4), 91(20.2), 93(4.4),
	97(70.2), 98(5.1), 99(8.1), 101(4.8), 102(4.7),
	103(5.9), 105(3.6), 108(3.8), 109(8.2), 110(5.3),
	111(8.9), 115(29.0), 116(4.8), 117(3.0), 121(10.6),
	122(4.0), 123(4.4), 127(14.0), 128(13.6),
	129(14.9), 133(3.1), 134(18.5), 135(10.0),
	136(3.0), 137(5.6), 139(5.1), 141(8.1), 142(10.8),
	143(4.7), 145(4.7), 147(19.1), 148(3.6), 149(14.4),
	151(5.1), 152(7.8), 153(6.1), 155(3.1), 158(4.2),
	159(5.1), 160(7.8), 161(14.2), 162(8.5), 163(6.5),
	165(10.4), 171(18.5), 172(6.8), 173(9.1), 174(5.5),
	175(16.5), 176(7.8), 177(19.9), 178(5.9), 179(5.1),
	184(18.3), 185(11.7), 186(5.5), 187(4.2), 189(7.8),
	190(6.5), 191(6.8), 192(4.4), 195(4.2), 197(7.6),
	198(7.8), 199(26.8), 200(8.7), 201(5.3), 203(4.2),
	205(4.8), 206(3.4), 210(3.6), 211(7.8), 213(6.8),
	214(4.0), 216(3.4), 217(5.6), 225(6.5), 226(4.4),

Compound No	Fragments, m/e (%)
(59)	227(3.1), 229(4.0), 230(3.6), 231(6.3), 232(4.7),
continued	233(11.4), 240(8.9), 241(5.5), 243(3.1), 244(5.1),
	245(7.6), 246(4.2), 247(3.1), 255(7.8), 256(3.8),
	259(15.1), 275(5.6), 289(53.1), 290(13.1), 291(6.3),
	304(26.5), 305(7.1).
(60)	14(11.5), 15(17.2), 16(14.8), 26(10.2), 27(31.8),
	28(63.5), 29(51.0), 31(12.5), 32(15.8), 39(36.4),
	40(14.7), 41(66.0), 42(17.1), 43(20.2), 45(39.0),
	47(5.7), 50(5.7), 51(12.6), 53(21.4), 54(6.8),
	55(17.1), 56(27.2), 57(100), 58(15.8), 59(18.4),
	60(4.6), 63(4.6), 64(4.6), 66(3.4), 67(10.2),
	69(21.4), 70(3.4), 71(9.2), 73(10.2), 74(10.2),
	75(8.0), 76(3.4), 77(19.4), 79(12.5), 83(3.4),
	84(5.7), 85(14.8), 86(17.2), 87(8.0), 88(15.8),
	89(3.4), 91(20.2), 92(9.2), 93(5.7), 94(3.4),
	96(5.7), 97(90.1), 98(12.5), 99(5.7), 100(3.4),
	101(4.6), 102(9.2), 103(9.2), 105(11.5), 106(4.6),
	108(11.5), 109(12.5), 110(8.0), 111(6.8), 113(3.4),
	114(4.6), 115(35.6), 116(6.8), 119(3.4), 120(4.6),
	121(22.9), 122(8.0), 126(4.6), 127(15.8), 128(22.9),
	129(8.0), 131(5.7), 132(3.4), 133(3.4), 134(21.4),
	135(14.8), 136(4.6), 137(3.4), 138(6.8), 141(9.2),
	142(11.5), 143(4.6), 145(5.7), 146(9.2), 148(8.0),
	149(12.5), 150(5.7), 151(8.0), 152(6.8), 153(14.8),
	156(5.7), 158(8.0), 159(13.8), 160(6.8), 161(12.5),
	162(5.7), 163(11.5), 165(11.5), 166(9.2), 167(3.4),
	171(21.4), 172(10.2), 173(9.2), 174(5.7), 175(21.4),
	176(5.7), 177(22.9), 178(13.8), 149(4.6), 183(4.6),
	184(17.5), 185(14.8), 186(11.5), 187(9.2), 188(4.6),
	189(13.8), 190(10.2), 191(14.8), 192(11.5), 193(3.4),
	195(5.7), 197(11.5), 198(9.2), 199(18.4), 200(11.5),
	201(5.7), 202(3.4), 203(5.7), 204(5.7), 207(5.7),
	208(4.6), 209(3.4), 210(5.7), 211(5.7), 213(13.8),
	215(5.7), 216(5.7), 217(4.6), 221(6.8), 223(3.4),
	225(3.4), 226(5.7), 227(3.4), 228(8.0), 230(8.0),
	231(3.4), 232(13.8), 233(3.4), 234(4.6), 239(5.7),
	240(3.4), 241(4.6), 242(5.7), 244(9.2), 246(6.8),

Compound No	Fragments, m/e (%)
(60)	255(10.2), 256(9.2), 259(13.8), 260(4.6), 261(4.6),
continued	262(4.6), 273(4.6), 274(5.7), 275(4.6), 289(45.9),
	290(15.8), 291(8.0), 304(27.6), 305(5.7), 306(5.6).

1,2-Di(2-thienyl)ethylenes

a) Halogen derivatives

(56)	45(16.2), 62(3.5), 63(5.6), 69(7.7), 74(3.2),
cis	82(3.2), 93(4.2), 95(16.2), 102(4.6), 114(3.2),
	145(16.9), 146(8.8), 158(3.5), 189(4.2), 190(100),
	191(13.4), 192(10.4), 269(3.7), 271(4.2), 348(18.0),
	350(35.6), 351(4.9), 352(20.0).
(56)	45(12.9), 63(4.8), 69(6.1), 82(3.4), 87(10.2),
trans	93(11.6), 94(8.2), 95(49.6), 96(5.4), 98(3.4),
	101(4.8), 102(8.8), 113(4.0), 114(5.4), 145(20.4),
	146(10.2), 158(4.1), 189(4.8), 190(100), 191(13.6),
	192(10.2), 269(4.1), 271(4.8), 348(17.0), 350(33.4),
	351(5.4), 352(19.8).
(25)	38(3.0), 39(8.2), 45(26.4), 50(5.0), 51(5.0),
	58(4.2), 62(6.0), 63(12.4), 69(15.4), 70(3.2),
	74(5.0), 75(4.6), 77(4.6), 82(5.8), 83(3.0),
	87(4.0), 89(6.6), 93(5.8), 95(21.6), 96(4.8),
	102(11.0), 103(4.4), 108(5.0), 113(4.0), 114(8.2),
	115(3.2), 120(3.6), 121(7.4), 134(3.8), 135(3.2),
	136(3.0), 145(15.6), 146(9.2), 147(98.0), 148(11.2),
	149(5.0), 158(14.8), 188(6.6), 189(94.0), 190(100),
	191(20.0), 192(9.0), 270(76.0), 271(9.8), 272(78.0),
	273(9.6), 274(7.0).
(27)	39(11.0), 45(26.3), 50(3.8), 51(6.2), 62(5.0),
	63(11.2), 69(15.0), 70(3.8), 74(3.8), 75(3.8),
	77(3.8), 82(5.0), 83(3.8), 84(5.0), 87(3.8), 89(5.0)
	93(5.0), 95(10.5), 96(8.7), 97(23.0), 98(3.8),
	102(6.3), 108(3.8), 109(3.8), 111(15.0), 114(6.3),
	115(5.0), 121(7.5), 124(8.8), 134(3.7), 135(3.7),
	145(14.0), 146(6.5), 147(31.3), 148(3.8), 158(8.8),

Compound No	Fragments, m/e (%)
(27)	179(3.1), 190(38.5), 191(76.5), 192(13.5), 193(8.5),
continued	203(3.7), 207(3.7), 219(5.0), 236(100), 237(15.0), 238(12.5).
(28)	39(10.3), 45(25.0), 50(3.7), 51(5.9), 58(5.2), 62(4.4), 66(10.3), 69(13.2), 74(3.7), 75(3.7), 77(4.4), 82(5.2), 84(3.7), 87(3.7), 89(4.4), 93(4.4), 95(9.6), 96(6.6), 97(19.1), 102(5.9), 103(3.7), 108(4.4), 109(3.7), 111(14.0), 114(5.2), 115(4.4), 121(7.4), 124(4.4), 134(3.7), 135(4.4), 139(18.4), 145(14.0), 146(6.6), 147(29.4), 148(3.7), 158(7.4), 179(3.7), 189(4.4), 190(35.2), 191(74.0), 192(13.2), 193(8.1), 207(5.2), 219(5.9), 236(100), 237(14.0), 238(11.0).

1,2-Di(3-thienyl)ethanes

a) Halogen derivatives

(3)	39(11.5), 41(33.5), 42(34.0), 43(20.0), 45(20.0), 51(5.5), 55(8.0), 56(4.5), 57(20.5), 63(3.0), 69(8.5), 70(9.5), 82(4.0), 95(7.5), 96(20.0), 147(7.5), 175(81.5), 176(5.5), 177(84.5), 178(4.5), 190(7.0), 191(40.5), 192(100), 193(17.5), 194(14.5), 271(25.0), 272(4.0), 273(26.5), 274(3.5).
(71)	26(6.6), 27(44.0), 28(14.6), 29(75.6), 30(3.7), 31(74.6), 38(5.1), 39(25.1), 40(4.8), 41(92.0), 42(36.5), 43(69.6), 44(6.0), 45(5.2), 50(4.4), 51(6.3), 53(4.6), 55(10.6), 56(51.9), 57(100), 58(3.8), 59(34.8), 69(8.1), 70(4.3), 73(3.9), 74(28.0), 82(3.7), 84(9.7), 85(4.3), 86(12.0), 95(4.3), 96(9.3), 97(8.6), 113(3.2), 175(28.5), 176(4.0), 177(29.4), 178(3.7), 190(5.4), 191(8.0), 192(26.4), 193(8.3), 194(7.3), 271(12.8), 273(13.8).

Compound No	Fragments, m/e (%)
(<u>9</u>)	39(6.0), 45(20.8), 51(4.0), 53(7.6), 69(5.6), 70(4.0), 95(3.2), 96(7.2), 97(100), 98(6.0), 99(4.0), 147(4.8), 160(7.2), 175(19.2), 177(20.0), 191(5.6), 193(100), 194(17.2), 195(10.0).
(<u>37</u>)	38(3.7), 39(8.2), 45(30.5), 50(4.9), 51(10.0), 63(5.1), 69(14.0), 70(7.1), 73(4.1), 79(16.6), 81(10.4), 82(5.8), 84(3.3), 85(4.5), 93(3.8), 95(13.2), 96(21.6), 97(13.8), 98(3.0), 107(3.3), 109(3.8), 121(6.1), 123(4.0), 131(6.9), 133(3.2), 145(4.4), 147(4.2), 165(71.2), 166(5.5), 167(49.2), 168(4.1), 169(9.5), 175(97.6), 176(7.5), 177(100), 178(7.9), 179(5.9), 189(3.0), 190(11.2), 191(7.9), 192(5.5), 225(10.8), 226(46.6), 227(15.3), 228(18.2), 229(5.3), 261(53.0), 262(8.2), 263(38.1), 264(5.5), 265(9.1), 304(5.3), 305(9.1), 306(8.3), 307(12.2), 308(3.7), 309(4.0), 340(5.4), 342(8.8), 344(4.5).
b) <u>Carboxylic acid derivatives</u>	
(<u>12</u>)	39(3.8), 45(17.7), 54(6.5), 69(3.6), 85(5.7), 97(13.5), 98(100), 99(10.0), 100(5.2), 141(6.5), 154(3.8), 206(3.0), 221(5.2), 237(3.2), 238(33.6), 239(5.9), 240(3.2).
(<u>19</u>)	39(4.2), 45(13.2), 53(6.5), 69(3.8), 97(100), 98(9.2), 99(5.5), 272(17.5), 274(7.4).
(<u>38</u>)	36(3.9), 39(10.8), 41(3.9), 45(40.3), 50(3.9), 51(8.8), 53(4.9), 63(6.0), 69(12.8), 70(5.9), 73(3.9), 79(16.7), 81(9.8), 82(3.9), 85(36.3), 87(3.9), 93(3.9), 95(9.8), 96(4.9), 97(32.5), 98(5.9), 107(3.0), 110(3.0), 121(5.9), 123(3.0), 131(3.9), 139(10.8), 141(100), 142(8.9), 143(6.9), 145(3.9), 165(60.0), 166(3.9), 167(40.0), 169(7.8), 190(11.0), 191(8.0), 192(4.9), 224(3.9), 225(5.9), 226(3.9), 227(4.9), 253(3.9), 270(23.5), 271(31.4), 272(17.6), 273(13.7), 274(3.9), 306(17.6), 308(12.7), 310(3.0).

Compound No	Fragments, m/e (%)
(<u>52</u>)	27(3.3), 39(7.4), 45(30.2), 51(6.2), 63(3.6), 69(7.4), 70(3.8), 73(3.8), 79(5.0), 81(3.2), 85(16.0), 87(4.5), 95(6.2), 96(5.0), 97(4.3), 131(100), 132(6.4), 133(38.1), 134(3.6), 135(3.3), 139(5.2), 141(40.6), 142(3.3), 147(4.3), 190(6.4), 191(9.5), 192(3.3), 193(7.6), 219(6.4), 236(24.3), 237(40.5), 238(8.1), 239(4.3), 272(9.1), 274(3.8).

1,2-Di-(2-thienyl)ethanes

(<u>26</u>)	28(10.4), 31(3.7), 39(6.7), 44(17.0), 45(22.0), 51(3.7), 53(8.8), 63(3.7), 69(5.2), 96(5.2), 97(100), 98(7.4), 99(5.2), 175(16.3), 177(17.8), 193(27.7), 194(3.7), 195(3.0), 272(2.2), 274(1.9).
(<u>29</u>)	39(3.5), 45(12.7), 53(6.2), 86(4.2), 97(100), 98(5.8), 99(4.3), 141(7.6), 238(17.8), 239(2.7), 240(2.0).

Cycloheptadithiophene systems

a) Dihydro-cycloheptadithiophene-ones

(d- <u>13</u>)	39(6.1), 40(3.3), 45(12.3), 51(4.0), 52(3.0), 63(4.0), 69(10.1), 70(11.8), 71(3.1), 82(3.1), 95(4.0), 96(8.1), 97(6.5), 116(5.6), 121(3.0), 122(3.3), 135(3.0), 146(3.3), 147(6.5), 148(33.2), 149(5.6), 159(4.5), 160(3.3), 178(3.4), 188(11.7), 190(5.4), 191(27.0), 192(68.7), 193(29.9), 194(9.8), 204(3.7), 206(3.0), 219(4.5), 220(35.1), 221(100), 222(19.4), 223(11.1).
(<u>33</u>)	39(7.2), 45(17.1), 50(3.7), 51(11.0), 52(3.1), 62(3.5), 63(7.9), 69(14.0), 70(9.3), 73(4.6), 74(3.1), 79(4.5), 81(3.6), 82(3.8), 87(3.3), 93(5.9), 95(26.0), 96(16.5), 97(4.6), 102(3.5), 109(3.6), 113(28.0), 114(3.3), 121(3.1), 130(4.8),

Compound No	Fragments, m/e (%)
(33)	132(3.0), 134(4.0), 145(9.8), 146(5.4), 147(26.6),
continued	148(4.2), 158(12.3), 181(7.8), 187(6.2), 189(4.4),
	190(44.6), 191(38.1), 192(14.5), 193(6.1),
	218(17.7), 219(51.0), 220(17.5), 221(39.0),
	222(7.5), 223(13.3), 224(4.3), 225(10.2), 226(4.9),
	227(4.5), 237(7.5), 239(6.4), 253(25.0), 254(100),
	255(24.2), 256(42.0), 257(6.7), 258(4.2).
(d-30)	39(4.4), 45(15.2), 46(3.1), 51(4.6), 52(4.1),
	63(5.0), 69(6.7), 70(9.0), 71(3.4), 95(4.4),
	96(11.5), 97(9.2), 116(6.7), 147(7.1), 148(26.2),
	149(5.4), 159(4.5), 160(5.1), 178(4.5), 187(7.0),
	188(40.6), 189(8.6), 190(6.6), 191(20.0), 192(42.0),
	193(14.5), 194(5.9), 204(9.6), 206(4.6), 219(6.4),
	220(48.0), 221(100), 222(24.8), 223(11.1).
(39)	45(6.6), 69(5.5), 70(3.1), 79(3.6), 93(3.6),
	94(3.3), 95(8.1), 96(7.5), 109(3.1), 112(4.0),
	129(7.3), 131(3.1), 145(10.0), 174(5.1), 179(3.5),
	181(4.2), 189(6.3), 190(29.8), 191(5.8), 192(8.8),
	217(3.5), 218(10.5), 224(16.2), 225(17.3), 226(9.7),
	227(9.0), 252(7.1), 253(69.0), 254(14.1), 255(43.3),
	256(7.1), 257(13.4), 258(3.6), 259(7.0), 260(7.5),
	261(4.6), 262(5.0), 273(5.8), 275(3.9), 287(5.9),
	288(100), 289(19.3), 290(75.8), 291(11.4), 292(17.7).
(54)	39(6.1), 45(14.1), 51(4.8), 63(4.6), 69(7.0),
	70(4.8), 82(3.0), 95(6.9), 96(8.6), 110(3.7),
	115(8.0), 121(4.5), 145(3.7), 147(12.1), 158(6.0),
	159(10.8), 173(3.0), 176(9.6), 187(40.5), 188(6.6),
	189(3.8), 190(15.1), 191(40.0), 192(14.2), 193(5.2),
	205(13.2), 219(19.8), 220(100), 221(17.0), 222(11.3).
	b) <u>Cycloheptadithiophene-ones</u>
(d-31)	45(8.5), 63(4.3), 64(3.0), 69(9.9), 82(5.8),
	93(5.5), 94(3.0), 95(4.1), 96(3.8), 102(3.3),
	103(7.4), 115(5.7), 145(5.5), 146(17.3), 147(10.4),
	159(7.0), 190(13.8), 191(100), 192(16.1), 193(10.7),

Compound No	Fragments, m/e (%)
(d- <u>31</u>)	218(9.3), 219(85.5), 220(14.4), 221(9.2).
continued	
(<u>32</u>)	45(14.0), 62(3.2), 63(6.0), 69(9.4), 73(3.5), 74(4.3), 75(3.4), 82(5.6), 87(4.5), 93(5.1), 94(3.2), 95(14.3), 101(3.4), 102(6.9), 109(7.5), 113(3.5), 114(5.6), 145(17.6), 146(9.0), 158(4.9), 189(3.4), 190(81.3), 191(10.9), 192(9.0), 218(100), 219(14.4), 220(10.2).
(d- <u>32</u>)	45(14.2), 62(3.0), 63(5.1), 64(3.6), 69(9.4), 74(3.4), 75(3.6), 82(3.9), 93(5.1), 95(3.8), 96(3.6), 102(4.4), 103(8.2), 114(3.8), 115(6.4), 145(5.9), 146(19.0), 147(11.0), 159(5.2), 190(15.1), 191(91.0), 192(19.2), 193(10.1), 218(13.2), 219(100), 220(21.3), 221(11.6).
(<u>80</u>)	45(8.3), 63(5.0), 69(6.7), 82(5.0), 93(3.6), 95(9.1), 102(5.1), 109(5.8), 114(5.9), 145(18.3), 146(8.5), 158(5.3), 189(4.2), 190(45.6), 191(6.4), 192(4.6), 218(100), 219(14.9), 220(11.4).
c) <u>Cycloheptadithiophenes</u>	
(<u>81</u>)	45(4.2), 69(4.6), 102(4.2), 115(5.4), 158(4.4), 171(10.2), 203(100), 204(59.3), 205(17.1), 206(5.6).
(<u>82</u>)	45(5.8), 63(3.0), 69(5.5), 80(3.0), 102(6.4), 115(6.4), 158(5.0), 171(10.9), 203(100), 204(61.9), 205(17.3), 206(6.5).
d) <u>Dithienotropylium perchlorates</u>	
(<u>84</u>)	18(10.1), 35(3.0), 36(15.0), 38(5.4), 44(17.8), 45(9.3), 62(3.7), 63(5.8), 64(5.4), 69(11.6), 74(3.9), 75(3.2), 82(6.9), 86(3.0), 87(3.9), 93(7.1), 94(4.7), 95(14.6), 101(4.3), 102(8.4), 113(3.2), 114(5.6), 120(3.4), 144(3.0), 145(32.0), 146(14.8), 147(3.2), 158(7.7), 189(18.0), 190(100), 191(14.6), 192(10.7), 203(15.0), 204(7.9), 217(18.0), 218(89.4), 219(13.7), 220(10.9), 224(4.7), 252(4.5).

Compound No Fragments, m/e (%)

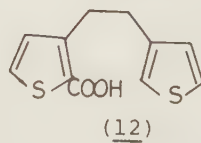
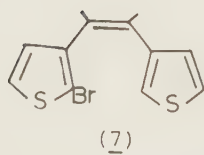
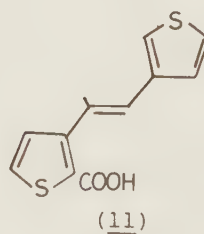
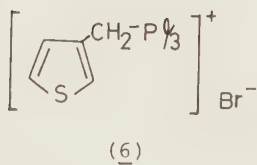
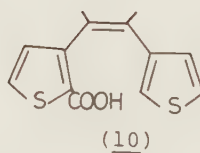
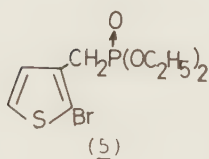
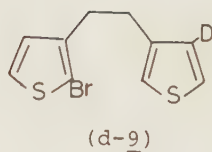
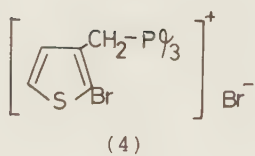
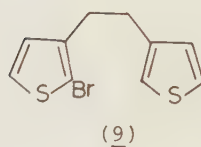
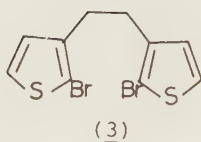
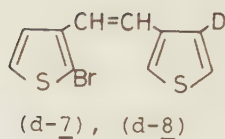
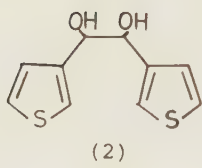
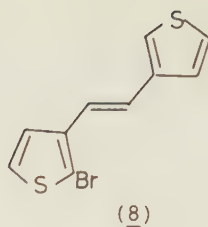
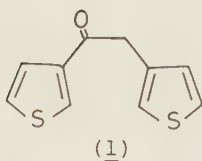
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48(3.0), 51(3.6), 52(3.4), 62(4.5), 63(6.4),
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95(6.1), 96(4.6), 102(5.8), 103(8.7), 114(4.2),
115(6.1), 120(3.1), 145(11.7), 146(21.7),
147(13.9), 148(3.6), 159(7.2), 189(4.5), 190(30.4),
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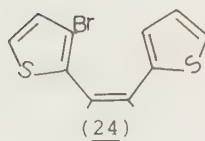
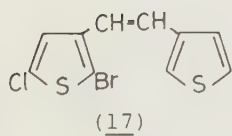
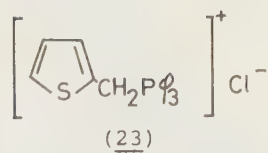
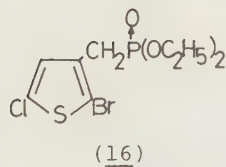
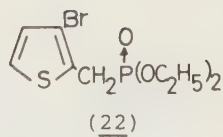
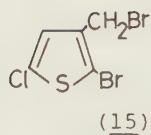
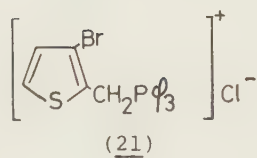
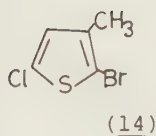
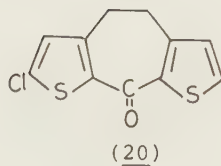
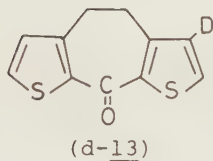
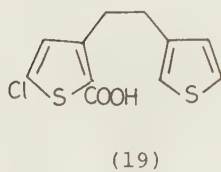
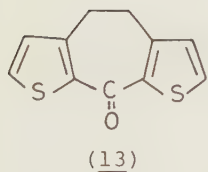
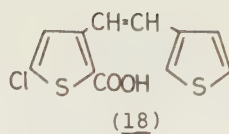
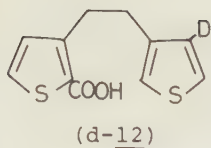
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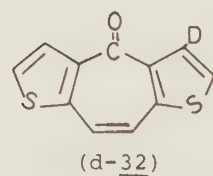
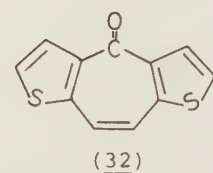
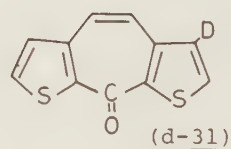
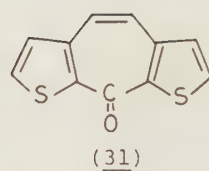
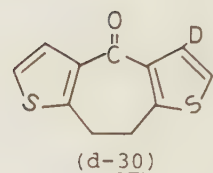
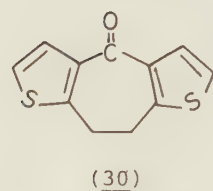
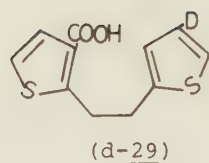
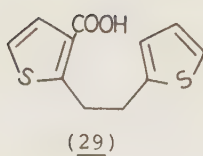
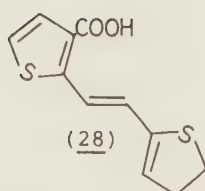
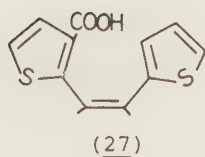
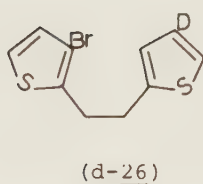
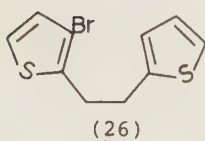
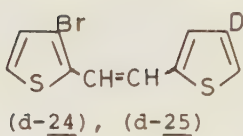
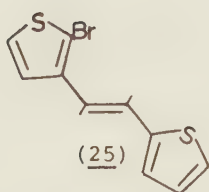
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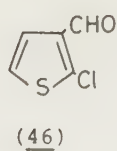
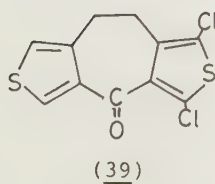
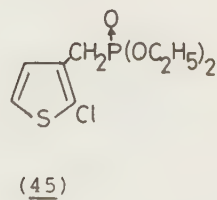
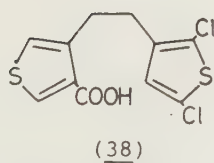
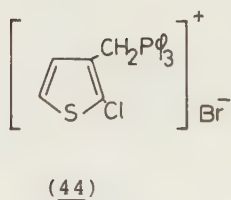
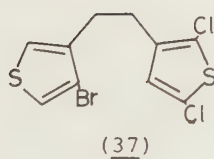
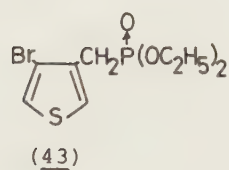
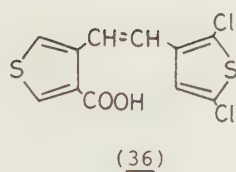
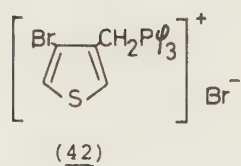
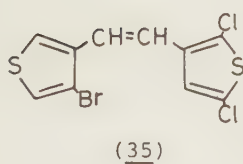
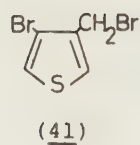
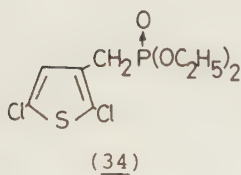
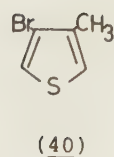
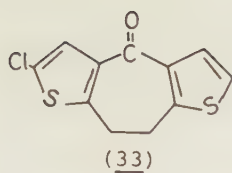
Compound No	Fragments, m/e (%)
(d- <u>85</u>)	202(15.6), 203(16.9), 204(100), 205(59.5), 206(19.5)
continued	207(9.1), 218(15.6), 219(88.5), 220(20.7), 221(10.4)
	235(3.3).

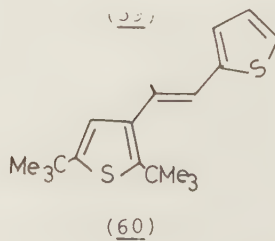
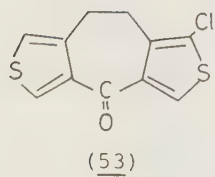
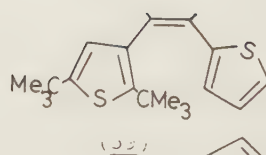
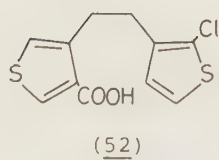
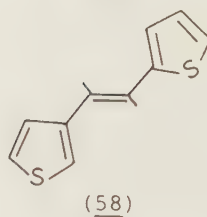
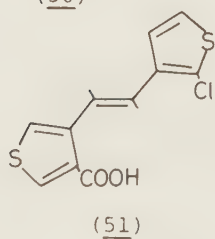
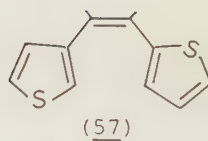
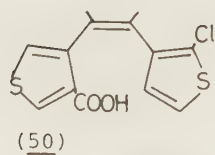
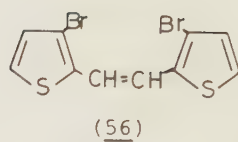
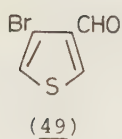
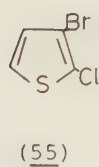
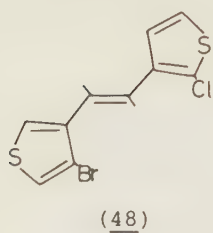
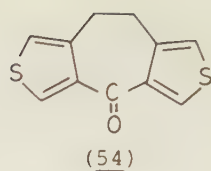
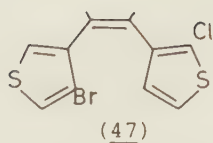
FORMULA INDEX
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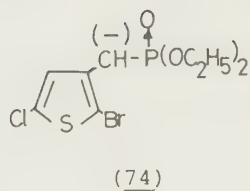
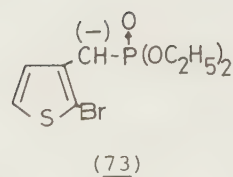
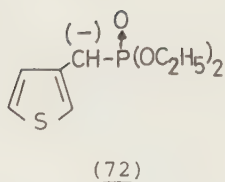
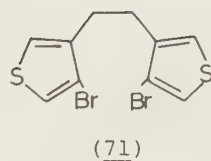
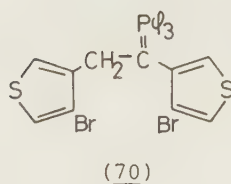
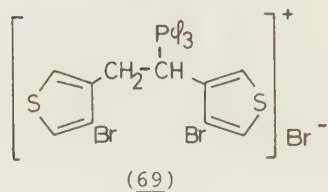
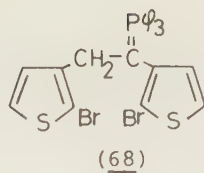
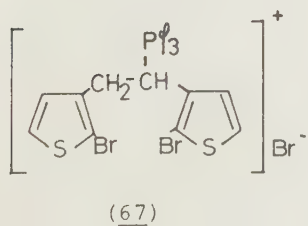
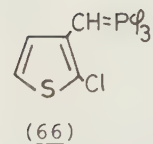
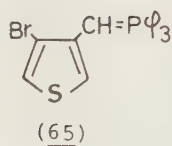
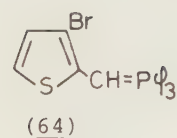
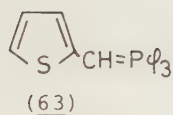
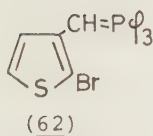
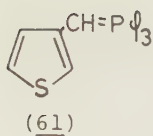


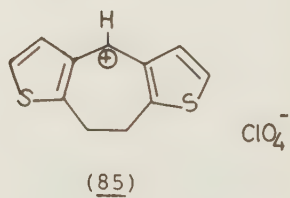
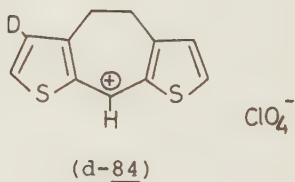
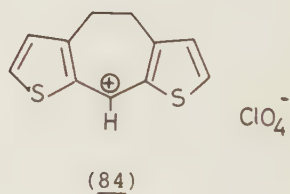
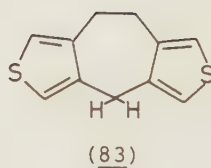
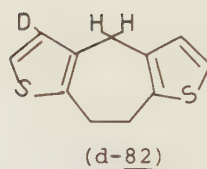
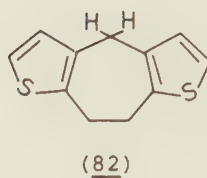
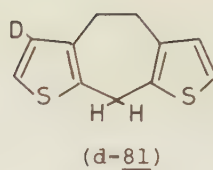
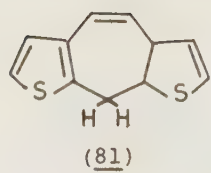
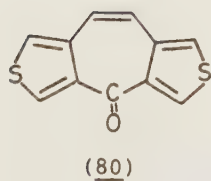
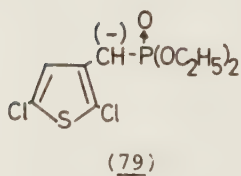
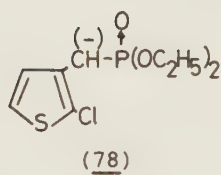
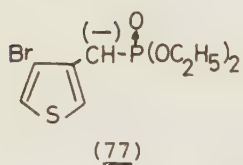
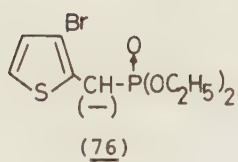
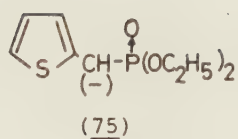


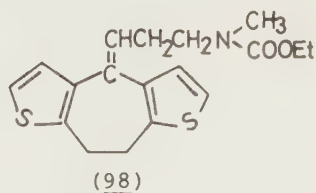
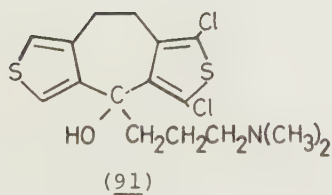
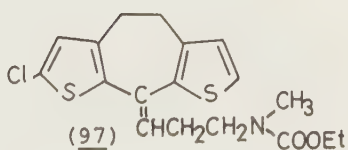
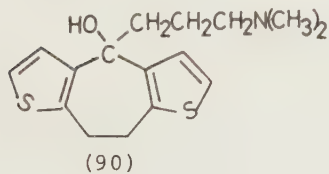
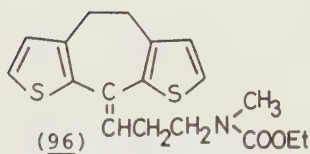
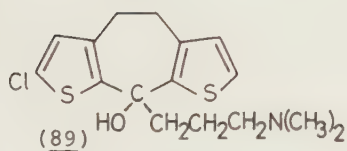
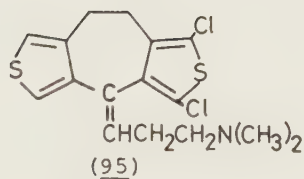
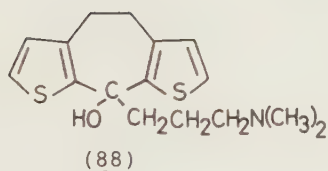
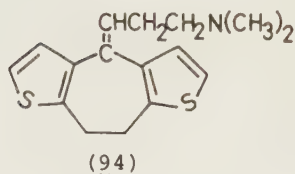
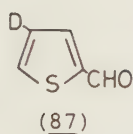
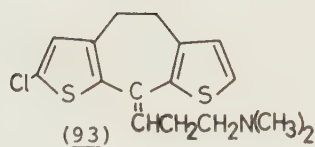
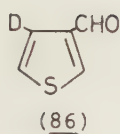
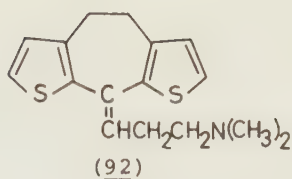
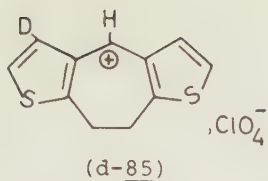


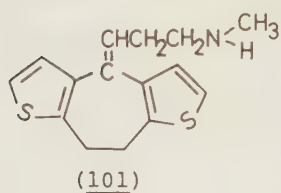
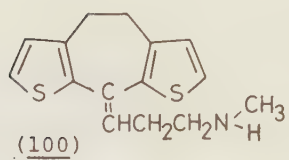
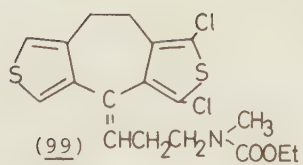












LITERATURE

- (1) S. Gabriel and A. Michael, Chem. Ber. 11, 1007 (1878).
- (2) W. Treibs and H.I. Klinkhammer, Chem. Ber. 83, 367 (1950).
- (3) W. Treibs and H.I. Klinkhammer, Chem. Ber. 84, 671 (1951).
- (4) E.D. Bergmann, E. Fischer, D. Ginsburg, Y. Hirshberg,
D. Lavie, M. Mayot, A. Pullman and B. Pullman,
Bull. Soc. Chim. France p. 684 (1951).
- (5) A.C. Cope and S.W. Fenton, J. Am. Chem. Soc. 73, 1673 (1951).
- (6) T.W. Campbell, R. Ginsig and H. Schmid, Helv. Chim. Acta
36, 1489 (1953).
- (7) V. Mychajlyszyn and M. Protiva, Coll. Czech. Chem. Comm.
24, 3955 (1959).
- (8) F. Hoffmann-La Roche & Co., Belg. Pat. 577 057 A.G. (1959).
- (9) Merck & Co., Inc., Belg Pat. 578 122, 582 220 and 584 061
(1959, 1960 and 1960b).
- (10) M. Protiva, V. Hněvsová-Seidlová, Z.J. Vejdělek,
I. Jirkovský, Z. Votava and J. Metysůvá, J. Med. Pharm
Chem. 4, 411 (1961).
- (11) S.O. Winthrop, M.A. Davis, G.S. Myers, J.G. Gavin,
R. Thomas and R. Barber, J. Org. Chem. 27, 230 (1962).
- (12) C.I. Judd, A.E. Drukker and J.H. Biel, U.S. Pat.
2 985 660 (1961). C.A. 65, 20078-9 (1966).
- (13) Merck & Co., Inc., C.A. 63 1757 (1965), and C.A. 65,
18544 (1966).
- (14) E.L. Engelhardt, M. E. Christy, C. Dylion Colton,
M.B. Freedman, C.C. Boland, L.M. Halpern, V.G. Vernier
and C.A. Stone, J. Med. Chem. 11 (2), 325 (1968).
- (15) R.D. Hoffsommer, D. Taub and N.L. Wendler, J. Org. Chem.
27, 4134 (1962).
- (16) G. Berti, J. Org. Chem. 22, 230 (1957).
- (17) N.C. Deno, J.J. Jaruzelski and A. Schriesheim,
J. Am. Chem. Soc. 77, 3044 (1955).

- (18) J.M. Bastian, A. Ebnöther, E. Jucker, E. Rissi and A.P. Stoll, *Helv. Chim. Acta* 49, 214 (1966).
- (19) J.M. Bastian, A. Ebnöther, E. Jucker, E. Rissi and A.P. Stoll, *Ibid.* 54, 277 (1971).
- (20) G.D. Kolomnikova and Z.N. Parnes "Advances in Chemistry of Tropylium Ion", *Russian Chem. Rev.* 36, 735 (1967).
- (21) E. Hückel, *Z. Physik* 70, 204 (1931).
- (22) W-E. Doering and L.H. Knox, *J. Am. Chem. Soc.* 76, 3203 (1954).
- (23) D. Meuche, H. Strauss and E. Heilbronner, *Helv. Chim. Acta* 41, 57 (1958).
- (24) H.H. Renhard, E. Heilbronner and A. Eschenmoser, *Chem. & Ind.* p. 415 (1955).
- (25) G. Navill, H. Strauss and E. Heilbronner, *Helv. Chim. Acta* 43, 1221 (1960).
- (26) M. Stiles and A.J. Libby, *J. Org. Chem.* 22, 1243 (1957).
- (27) R.G. Turnbo, D.L. Sullivan and R. Pettit, *J. Am. Chem. Soc.* 86, 5630 (1964).
- (28) S. Gronowitz, "Recent Advances in Chemistry of Thiophenes", *Advances in Heterocyclic Chemistry Vol 1* p. 1. Edited by A.R. Katritzky. Academic Press, New York 1963.
- (29) *Heterocyclic Compounds Vol 2* p 147. Editor Robert C. Elderfield. John Wiley & Sons, Inc., New York.
- (30) H. Wynberg, J. de Wit and H.J. Sinnige, *J. Org. Chem.* 35, 711 (1970).
- (31) a) D.S. Rao and B.D. Tilak, *J. Sci. Ind. Res. (India)* 17B, 260 (1958).
 b) D.S. Rao and B.D. Tilak, *Ibid.* 13B, 829 (1954);
 R.M. Kellogg, M.B. Broen and H. Wynberg,
J. Org. Chem. 32, 3093 (1967).
 c) D.S. Rao and B.D. Tilak, *J. Sci. Ind. Res. (India)* 16B, 65 (1957);
 C.E. Loader and C.G. Timmons, *J. Chem. Soc. (C)*
 p. 1677 (1967).
- (32) S. Gronowitz, P. Gassne and B. Yom-tov, *Acta Chem. Scand.* 23, 2927 (1969).

- (33) A. Jeffries, Private communication.
- (34) E. Campaigne and W.M. LeSuer, J. Am. Chem. Soc. 70, 1555 (1948).
- (35) U. Michael, Private communication.
- (36) I.N. Nazarov and I.L. Kotlyarevskii, C.A. 45, 1963h.
- (37) T.F. Dankova, T.N. Bokova, N.A. Preobrazhenskii, A.E. Petrushchenko, I.A. Il'shtein and N.I. Shvetsov, C.A. 45 9517f.
- (38) B.R. Brown and A.M.S. White, J. Chem. Soc. p. 3755 (1957).
- (39) D.H. Wadsworth, O.E. Schupp, E.J. Sens and J.A. Ford, J. Org. Chem. 30, 680 (1965).
- (40) A.-B. Hörnfeldt, J.S. Gronowitz and S. Gronowitz, Acta Chem. Scand. 22, 2725 (1968).
- (41) J.A. Osborn, F.H. Jardine and G. Wilkinson, J. Chem. Soc. (A) p. 1711 (1966).
- (42) K. Ditmer, R.P. Martin, W. Hertz and S.J. Cristol, J. Am. Chem. Soc. 71, 1202 (1949).
- (43) U. Michael and S. Gronowitz, Acta Chem. Scand. 22, 1353 (1968).
- (44) U. Michael, Ph.D. Thesis, University of Lund 1971.
- (45) S. Gronowitz, Ark. Kemi 8, 441 (1955).
- (46) S. Gronowitz, A. Biezais and B. Mattiasson, Ark. Kemi 21, 279 (1963).
- (47) D.W.H. MacDowell, T.B. Patrick, B.D. Frame and D.L. Ellisson, J. Org. Chem. 32, 1226 (1967).
- (48) E. Campaigne and W.M. LeSuer, J. Am. Chem. Soc. 71, 333 (1949).
- (49) S. Gronowitz, P. Moses, A.-B. Hörnfeldt and R. Håkansson, Ark. Kemi 17, 173 (1961).
- (50) S. Gronowitz, P. Moses and R. Håkansson, Ark. Kemi 16, 267 (1960).
- (51) W. Steinkopf and H. Jacob, Ann. 515, 273 (1935).
- (52) J. de Wit, Private communication, University of Lund 1969, Lund, Sweden.
- (53) G. Wittig and U. Schöllkopf, Chem. Ber. 87, 1318 (1954).
- (54) F. Bohlmann, E. Inhoffen and P. Herbst, Chem. Ber. 90, 1661 (1957).
- (55) L.D. Bergelson and M.M. Shemyakin, Tetrahedron 19, 149 (1963).

- (56) L.D. Bergelson and M.M. Shemyakin, *Angew. Chem.* 76, 113 (1964).
- (57) L.D. Bergelson, V.A. Vaver, L.I. Barsukov and M.M. Shemyakin, *Tetrahedron Letters* p. 2357 (1965).
- (58) H.O. House and G.R. Rasmusson, *J. Org. Chem.* 26, 4278 (1961).
- (59) A. Maerker, "The Wittig Reaction", *Organic Reactions* Vol 14, p. 270. John Wiley and Sons, Inc., New York 1965.
- (60) M. Schlosser, "The Stereochemistry of the Wittig Reaction" in *Topics in Stereochemistry*, E.L. Eliel and N.L. Allinger, Editors. Vol 5 p. 1-30. Wiley-Interscience, New York 1970.
- (61) S. Trippett, "The Wittig Reaction", *Pure and Applied Chemistry* 9, 255 (1964).
- (62) G.H. Birum and C.N. Matthews, *J. Org. Chem.* 32, 3554 (1967); F. Ramirez, C.P. Smith and J.F. Pilot, *J. Am. Chem. Soc.* 90, 6726 (1968).
- (63) A.J. Speziale and D.E. Bissing, *J. Am. Chem. Soc.* 85, 3878 (1963).
- (64) H.O. House, V.K. Jones and J.A. Frank, *J. Org. Chem.* 29, 3327 (1964).
- (65) G.S. Hammond, *J. Am. Chem. Soc.* 77, 334 (1955).
- (66) R. Kecham, D. Jambotkar and L. Martinelly, *J. Org. Chem.* 27, 4666 (1962).
- (67) A.W. Johnson and V.L. Kyllingstad, *J. Org. Chem.* 31, 334 (1966).
- (68) K. Eiter and H. Oendinger, *Ann. Chem.* 682, 62 (1965).
- (69) L. Krombie, P. Hemesley and G. Pattenden, *J. Chem. Soc. (C)* p. 1024 (1969).
- (70) S. Gronowitz and J. de Wit, Unpublished results.
- (71) H.J. Bestmann, R. Hörlt and H. Häberlein, *Ann. Chem.* 718, 33 (1968).
- (72) L. Horner, H. Hoffmann, H. Wipple and G. Klahre, *Chem. Ber.* 92, 2499 (1958).
- (73) L. Horner, *Fortschr. Chem. Forsch.* 7, 1 (1966).
- (74) H.J. Dauben, Jr., F.A. Gadecki, K.M. Harmon and D.L. Pearson, *J. Am. Chem. Soc.* 79, 4557 (1957).
- (75) Jaffé and Orchin, "Theory and Application of UV Spectroscopy" p. 443. John Wiley and Sons, Inc., New York 1962.

- (76) A. Streitwieser, Jr., "Molecular Orbital Theory for Organic Chemists" Chapter 12. John Wiley and Sons, Inc., New York 1961.
- (77) B. Aurivillius, Div. of Inorganic Chemistry II, University of Lund, Private communication.
- (78) S. Ross, Astra Pharmaceuticals, Sweden, Private communication.
- (79) M. Protiva, M. Rajsner, E. Adlerová, V. Seidlová and Z.J. Vejdělek, Coll. Czch. Chem. Comm. 29, 2161 (1964).
- (80) K. Stach and F. Bickelhaupt, Monatsh. Chem. 93, 896 (1962).
- (81) R.M. Kellogg, A.P. Schaap, E.T. Harper and H. Wynberg, J. Org. Chem. 33, 2902 (1968).
- (82) K.B. Wiberg and H.F. McShane, Org. Synth. 29, 31 (1949).
- (83) H. Wynberg and A. Kraak, J. Org. Chem. 29, 2455 (1964).
- (84) E. Campaigne and W.M. LeSuer, J. Am. Chem. Soc. 70, 415 (1948).
- (85) R.M. Kellogg, M.B. Groen and H. Wynberg, J. Org. Chem. 32, 3093 (1967).
- (86) W.S. Wadsworth and W.D. Emmons, J. Am. Chem. Soc. 83, 1733 (1961).
- (87) B.P. Fabrichnyi, I.F. Shalavina, S.E. Zurabyan, Ya.L. Gol'dfarb and S.M. Kostrova, Zh. Org. Khim. 4, 680 (1968).

